THE USE OF COMPLEMENTARY AND ALTERNATIVE THERAPIES AMONG ADULT HIV POSITIVE PATIENTS IN AN OUTPATIENT SETTING

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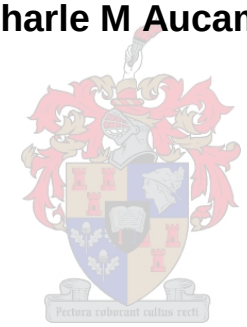

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DECLARATION

I, Charlé M Aucamp, declare that this thesis is my own original work and that all sources have been accurately reported and acknowledged, and that this document has not previously in its entirety or in part been submitted at any university in order to obtain an academic qualification.

Signature  Date: 20/02/08

ABSTRACT

Objective: To determine the use of complementary and alternative medicine (CAM) among adult HIV positive patients in an outpatient setting.

Design: A prospective, observational study performed on patients diagnosed with HIV. The study was conducted from July 2005 to November 2005.

Setting: An Outpatient clinic at the Department of Sexual Health (DOSH), Whipps Cross University Hospital, London.

Subjects: All patients diagnosed with HIV at the DOSH were approached to participate in the project. Data on patients not using CAM and incomplete questionnaires were not used in the data analysis process.

Outcomes measures: The outcome measures include the prevalence of CAM use, reasons for using CAM therapies and monthly expenditure with CAM therapies, sources of information about CAM therapies, disclosure of CAM therapy use, knowledge regarding antiretroviral therapy and CAM therapy drug interactions.

Results: Of the original 81 participants, 38 reported not using CAMs and could not complete the questionnaire. Thirty four participants completed full questionnaires. Seventy nine percent of participants reported that the main reasons for CAM therapy use were the general health advantages and putative effect on long-term survival. The most commonly used CAM therapy in this study were micronutrients (71%). Monthly out-of-pocket expenditure on CAM therapies was < £10 for most participants. No other statistically significant results were obtained from the questionnaire.

Conclusion: Results of this study suggest that CAM therapies are used by HIV infected patients to *complement* conventional treatment and not as an

alternative. Multivitamins and minerals were the most commonly used CAM therapy.

ABSTRAK

Doel: Om die gebruik van aanvullende en alternative terapieë (AAT) onder volwasse MIV positiewe pasiënte in ‘n buite-pasiënte omgewing te bepaal.

Studie ontwerp: ‘n Prospektiewe, waarnemende studie uitgevoer op pasiënte gediagnoseer met MIV. Die studie het plaasgevind gedurende die tydperk Julie 2005 tot November 2005.

Plek: ‘n Buite-pasiënt kliniek by die Departement van Seksuele Gesondheid (DOSH), Whipps Cross Universiteite Hospitaal, Londen.

Pasiënte: Alle pasiënte gediagnoseer met MIV by DOSH is genader om aan die projek deel te neem. Data van pasiënte wat nie AAT gebruik het nie, asook onvoltooide vraelyste is nie in die data-analise ingesluit nie.

Uitkomste: Die uitkomste sluit die gebruik van AAT, redes vir die gebruik en maandelikse koste van AAT, bronne van inligting rakende AAT en kennis aangaande interaksies tussen antiretrovirale terapie en AAT-gebruik in.

Resultate: Van die oorspronklike 81 deelnemers het 38 aangedui dat hulle geen AAT gebruik nie en kon nie die vraelys voltooi nie. Vier en dertig deelnemers het voltooide vraelyste ingevul. Nege-en sewentig persent van deelnemers het aangedui dat die hoofrede vir AAT gebruik was die algehele gesondheids-voordele en potensiele langtermyn oorlewing. Die mees algemene gebruikte AAT in hierdie studie was mikronutriente (71%). Maandelikse uitgawes op AAT terapie was ongeveer £10 vir meeste gebruikers.

Gevolgtrekkings: Resultate van hierdie studie dui aan dat MIV positiewe pasiente AAT gebruik om konvensionele behandeling te *komplimenteer* en nie as ’n *alternatiewe* behandeling nie. Multivitamiene en -minerale was die mees algemeenste gebruikte AAT.

DEDICATION

In ensuring that the millions

of people who are infected and affected

by HIV and Aids are not forgotten,

we will not only make a difference to their lives, we will

also make a difference to our lives as well. We owe this at

least to humanity.

Give one minute of your life to Aids.

-Nelson Mandela speaking at the 15th International AIDS Conference, Bangkok

15 July 2004

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I would like to take the opportunity to say a special thanks to all my work colleagues at the Department of Sexual Health, Whipps Cross Hospital, London for their support and encouragement in completing this thesis. Finally, thanks to my study leaders for their help and advice over the past few years.

LIST OF ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
ARV	Anti retroviral
CAM	Complementary and Alternative Medicine
CDC	Centre for Disease control and Prevention
CYP1A2	Cytochrome P450, family 1, subfamily A, polypeptide 2
CYP3A	Cytochrome P450, family 3, subfamily A
CYP3A4	Cytochrome P450, family 3, subfamily A, polypeptide 4
DHEA	Dehydroepiandrosterone
DOSH	Department of Sexual Health
DSHEA	Dietary Supplement Health and Education Act
EU	European Union
FSA	Food Standard Agency
GMP	Good Manufacturing Practice
HIV	Human Immunodeficiency virus
MHRA	Medicines and Healthcare products Regulatory Agency
MSM	Men who have sex with men
NAC	N-acetyl cysteine
NCCAM	National Centre for Complementary and Alternative Medicines
NHS	National Health Service
NNRTI	Non-nucleotide Reverse transcriptase inhibitors
OI	Opportunistic infections
PEM	Protein Energy Malnutrition
PI	Protease Inhibitor

PLWHA	People living with HIVAIDS
PXR	Pregnane X Receptor
SOPHID	Survey of Prevalent HIV Infections Diagnosed
UK	United Kingdom
US	United States

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CHAPTER 1: INTRODUCTION AND PROBLEM STATEMENT

1.1 Interrelations of HIV Disease, Nutritional Status and Prognosis

In the pre-Antiretroviral (ARV) treatment era, more than 60% of human immunodeficiency virus (HIV) infected people presented with protein energy malnutrition (PEM) and vitamin and mineral deficit.[1,2,3] This caused significant wasting/cachexia and increased susceptibility to opportunistic infections (OI) and drug toxicity.[1,2,3] The HIV wasting syndrome is defined as weight loss (>10% of usual body weight) with fever and/or diarrhoea of unknown origin.[4] Some wasting may even occur in the absence of these symptoms. Rapid wasting is usually a manifestation of OIs or malignancy in late Acquired Immunodeficiency Syndrome (AIDS) with advanced immunodeficiency. Weight loss of as little as 5%, specified in the Centre for Disease Classification Control and Prevention (CDC) definition may also have an adverse effect on disease progression.[5]

The introduction of ARV treatment in 1996 has decreased the incidence of wasting, and is now seen mostly in patients who have never been treated or where treatment has failed due to ARV drug resistance or intolerance. Appendix 1 provides an overview of ARV drugs currently available in the United Kingdom (UK) and licensed by the European Union (EU). [6]

In addition to wasting syndrome, lipodystrophy is also a common complication of ARV treatment especially protease inhibitors. Lipodystrophy manifests as fat redistribution with loss of subcutaneous fat, increase in intra-abdominal fat, buffalo hump or breast hypertrophy. Body weight may increase or decrease depending on the relation between subcutaneous lipoatrophy and intra-abdominal lipohypertrophy.[5]

The prognosis of advanced HIV infection is influenced by loss of body weight. Decreased nutritional status, characterised by loss of lean and fat mass, in HIV–infected patients is associated with an increased mortality, independently of immunodeficiency and viral load.[7]

The use of CAM has increased over the past decade [8, 9] and has been the focus of increased interest from patients, clinicians and investigators.[10] Approximately one in four persons in the United States (US) use CAM therapy [11] and it is estimated that 80% of the world's population use some form of herbal medicine as part of their primary health care.[12] A survey in 1989 in the UK showed that 74% of the public surveyed were in favour of CAM therapies being made widely available on the National Health Service (NHS). In any year it is estimated that 11% of the adult population in the UK visited a complementary therapist.[13]

Herbal products were among the most popular CAM therapies, with an estimated annual market of $5.1 billion.[14] A study by Eisenberg *et al.* (1993) revealed that over 30% of Americans have sought treatment from alternative health care practitioners and made more visits to these practitioners than conventional health care providers. High costs and potentially hazardous side effects of pharmaceutical drugs have been partly responsible for this trend.[15] The use of CAM therapy is also a common phenomenon among patients who suffer from chronic diseases that are either untreatable, or for which conventional medical therapy is only partially effective[16,17,18] Although CAM therapy use is often to the detriment of conventional medical approaches, it is commonly used in conjunction with conventional therapies.[8, 9]

One of the major problems with the use of CAM therapies is the lack of adequate research on its efficacy and safety. This applies particularly to herb-drug

interactions.[14] In the US, herbal products are regulated as dietary supplements under the 1994 Dietary Supplement Health and Education Act (DSHEA). This includes a framework for safety, labelling, third - party literature provided at the point of sale and good manufacturing practice (GMP). It is the manufacturer's responsibility to ensure that its products are safe and properly labelled prior to marketing. Undoubtedly herbal products are not subject to the same strict rules and regulations imposed on other over-the-counter and prescription medication. In the UK there are two main legal categories of therapeutic and nutritional products under which these products can be sold/manufactured:

1. **Licensed medicines**: some vitamin and mineral preparations are licensed by the Medicines and Healthcare products Agency (MHPA). All products are assessed for safety, efficacy and quality in accordance with UK and EU legislation. If approved, these products are granted Marketing Authorisation, which allows companies to make medicinal claims and assigned the appropriate licence status. These products are often indicated for the treatment of deficiency states (e.g. HIV – related malnutrition) [19]
2. **Unlicensed preparations**: Most vitamins, mineral and other supplements are treated like food products. They are therefore, controlled under food legislation by the Food Standards Agency (FSA) and policed by the local trading standards authorities. These companies are not permitted to make any medicinal claims related to their products, alleging therapeutic benefit for any disease .[19]

Therapeutic and nutritional supplements fall within this category of unlicensed preparations with a confusing overlap in ingredients, evidence base and routes of

supply. The public may use unlicensed products for therapeutic purposes, although companies are not required to demonstrate their efficacy before marketing, nor are these products subject to prior approval. The main requirements for food related products are safety and labelling according to EU guidelines. In addition, companies are not allowed to make medicinal claims, however health claims and functional claims are allowed.

As a result there is a lack of evidence based research regarding CAM's pharmacology, pharmacokinetics, drug interactions, efficacy and safety.[20]

1.2 Exploring CAM Therapies

Several factors influence the choice of CAM therapies. Patients who seek CAM therapy may be dissatisfied with conventional medical therapy, desire more control or autonomy over decisions involving their health, or see CAM as more compatible with their world's view and belief system.[21] Links with cultural beliefs were specifically found to impact on CAM choice, especially in people with a commitment to environmentalism, feminism, an interest in spirituality and personal growth psychology.[21, 22] Individual cultural background and ethnicity also influence CAM therapy use.[1]

Patients have been shown to engage in self-care practices using CAM therapies as true alternatives, thereby placing themselves at risk of delayed diagnosis with possible serious consequences.[23] There is a general misconception among the public that because a product is 'natural' it is safe, free from side effects and drug interactions.[19] Considering the widespread use of herbal remedies for various medical conditions, and with certain herbal remedies shown to be unsafe or

potentially unsafe, patients are at risk for both drug-related and disease-related problems that may be largely preventable.[23]

CAM therapies are a broad term, encompassing many unconventional practices including relaxation techniques, spiritual healing, massage, herbal therapy and dietary supplementation. The National Centre for Complementary and Alternative Medicine (NCCAM), in the US, defines CAM therapies as a group of diverse medical and healthcare systems, practices, and products that are not at present considered part of conventional medicine. Conventional medical therapies are defined as treatments that are widely taught in medical schools or generally available in hospitals.[20]

CAM therapies comprise two components namely:

- Complementary medicine, which is used **in addition to** conventional medicine
- Alternative medicine, which is used **in place of** conventional medical therapy

NCCAM classifies CAM therapies into: alternative medical systems, mind-body interventions, biologically based therapies, manipulative and body based methods and energy therapies (Figure 1.1).[24]

The Cochrane Collaboration (UK) defines CAM as “a broad domain of healing resources that encompasses all health systems, modalities, and practices and their accompanying theories and beliefs, other than those intrinsic to the politically dominant health systems of a particular society or culture in a given historical period”.[25]

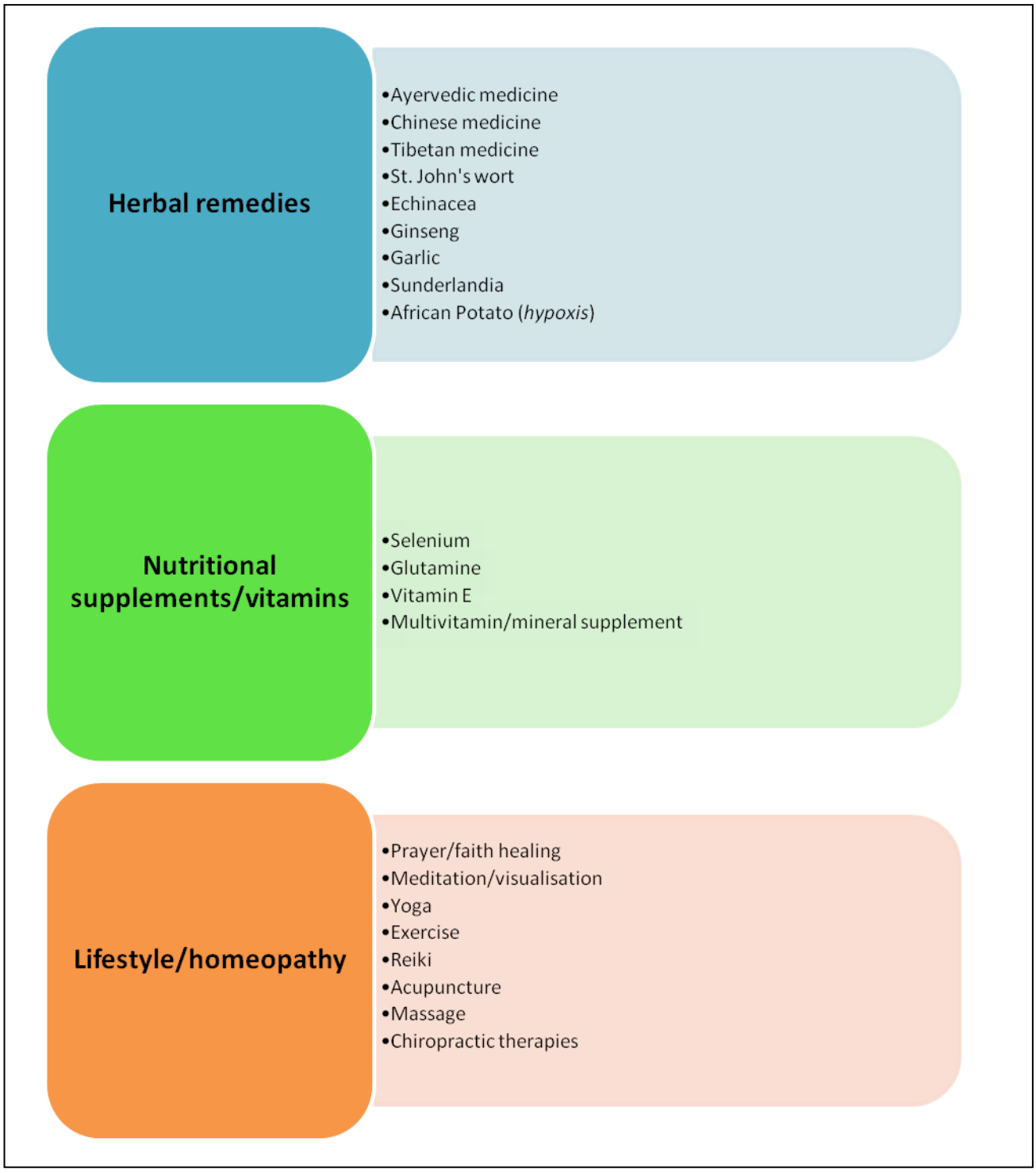

Figure 1.1: Classification of CAM therapies

1.3 CAM Therapies in HIV

At the beginning of the HIV epidemic little or no treatment was available for people infected with the disease. HIV-infected people primarily used CAM therapies that

allegedly had antiviral or immunostimulatory properties.[26] Over the past few years, investigators have identified a number of drugs that can slow down the progression of the disease as well as therapies to treat the OI.[35] ARV therapy and prophylactic medications for OI infections have increased the life expectancy for people living with HIV/AIDS.[35] However, due to their longevity, patients with HIV/AIDS, have more time to experience the side effects associated with ARV therapy as well as the disease itself.[27] The key to effective treatment of HIV infection remains early detection and intervention. Early treatment can strengthen the immune system, reduce stress, maintain good nutritional status and appropriate exercise regimes. Many of the CAM therapies place significant emphasis on these lifestyle issues.[37] CAM therapies in HIV management may take the form of meditation, massage, acupuncture, spiritual healing and other non-pharmacologic therapies, but it is usually associated with dietary supplements, vitamins and herbs.[20]

During the past few years the public's interest in alternative therapies has grown. It has been estimated that one in three Americans are currently using some form of alternative therapy and among people infected with HIV the proportion is even higher.[28] De Visser and colleagues [29] found that 56% of their sample (924 respondents) living with HIV/AIDS in Australia uses CAM therapies. A number of studies have suggested that over half of all HIV-positive men in the US who have sex with men (MSM)/bisexual men are using CAM therapies.[30]

1.4 Knowledge Regarding Antiretroviral and CAM Therapy Drug Interactions

Herbal products are commonly used for various purposes and can interact with the prescribed ARV drugs in the body (Table 1.1). These ARV drug - herb interactions can result in ARV drug resistance, drug toxicity, treatment failure and ARV treatment

side effects.[31] Many ARV medications, such as Protease Inhibitors (PIs) and Non–Nucleoside Reverse Transcript Inhibitors (NNRTIs), are predominantly metabolized through the Cytochrome P450, family 3, subfamily A, polypeptide 4 (CYP3A4) oxidative metabolic pathway and in the case of HIV PIs, are also substrates for drug transporters such as P-glycoprotein. Herbal therapies have been shown to affect the serum levels of ARV medication through their effects on CYP3A4 metabolism and P-glycoprotein.[32]

Table 1.1: Commonly used herbal products, purpose for use and known interactions.[33]

Herbal products	Purpose for use	Known interactions with ARV treatment	Outcome	Reference
St. John's Wort (*hypericum*)	Depression, anxiety and/or sleep disorders	Induces certain Cytochrome P450 drug-metabolizing enzymes in the liver (especially CYP1A2, CYP2C9 and CYP3A4) and P-glycoprotein (a transport protein). Indinavir (PI) and Nevirapine (NNRTI) are predominantly metabolized through CYP3A4 pathway.	Reduces the blood concentrations of Indinavir (PI) and Nevirapine (NNRTI) with possible loss of HIV suppression.	34, 35, 36
Echinacea	Prevent colds, flu and other infections Stimulate immune system to help fight infections	Causes inhibition of CYP1A2 and intestinal CYP3A activity and induction of hepatic CYP3A activity.	Could resulting in elevated levels of PIs with increased side effects	36
Garlic (*Allium sativum*)	Beneficial cardiovascular effect. The most common use in terms of HIV. Antibiotic properties	Possible induction of gut mucosal CYP450 3A4 by garlic; P-glycoprotein effects are also possible.	Decreased Saquinavir levels as most PIs are processed by CYP3A4. Therefore, higher than expected levels of the drug is in the body causing side-effects.	36, 42
Milk thistle (*Silybum marianum)*	Hepato-protective effects and therefore typically used for liver diseases such as cirrhosis and hepatitis.	Relatively small concentrations of milk thistle can significantly slow down the activity of the liver enzyme CYP3A4 by 50% to 100%.	Should not interfere with Indinavir therapy in patients infected with HIV. However, caution when using with other PI's and NNRTI's	41, 42, 43
Sutherlandia *Frutescens*	Have antioxidant and anti-inflammatory potentials	In-vitro inhibition of CYP3A4 and P-glycoprotein expression. Further in-vitro studies also demonstrated propensity for activation of PXR, a nuclear receptor that controls the activation of both CYP3A4 and P-glycoprotein	Possible induction of decreased drug exposure with prolonged therapy	38
Afican Potato (Hypoxis)	Immunostimulant	In-vitro inhibition of CYP3A4 and P-glycoprotein expression. Further in-vitro studies also demonstrated propensity for activation of PXR, a nuclear receptor that controls the activation of both CYP3A4 and P-glycoprotein	Possible induction of decreased drug exposure with prolonged therapy	38

1.4.1 St. John's Wort

The best-known example and most commonly used CAM therapy in HIV/AIDS patients in developed countries is St John's Wort (*Hypericum perforatum),* which has documented anti-depressant properties.[34] St. John's Wort is widely used by people with mild depression, often in combination with prescribed antidepressants. Two separate small studies done on healthy volunteers, have found that St John's Wort reduces the concentration of Indinavir [34] and Nevirapine [35] in the body.

Indinavir a PI, one of the most potent drugs available for treating HIV infection, has been shown to prolong survival and slow the progression of the disease[34]. Substances in both St. John's Wort and Indinavir share the Cytochrome P450 metabolic pathway, which suggest the probability of a drug interaction. Plasma levels of Indinavir have shown to be substantially reduced by the concomitant use of the herbal preparation St. John's Wort, to about 20% of those when Indinavir is given alone.[36] This may result in suboptimal antiretroviral drug concentrations, leading to loss of virologic failure and development of resistance or class cross-resistance.

A study was conducted in 176 HIV infected people who were using Nevirapine as part of their ARV treatment regimen. Five of these patients also used St John's Wort concurrently for several months. The study results indicated that the clearance of Nevirapine was significantly increased by 35%, thus lowering exposure to Nevirapine.[34] Therefore the use of Nevirapine together with St John's Wort (Hypericum) or St John's Wort containing products is not recommended.

Patients taking this specific PI and/or NNRTI's should avoid using St. John's Wort [34] as it demonstrates that this commonly used herb perceived to be harmless, may

have unsuspected adverse effects on a drug essential to the health of a very vulnerable population. As a result it is recommended that patients keep their doctor or pharmacist informed about any use of herbal products.[35]

1.4.2 Sutherlandia and African potato *(Hypoxis)*

Mills *et al.* (2005) analysed the effect of two herbs in common medical use in Africa, Sutherlandia and African Potato (*Hypoxis*) for their potential interactions with common antiretroviral agent metabolizing mechanisms *in vitro.*

Sutherlandia *frutescens* (common names: Insiswa*, Unwele, Mukakana, Phetola, Lerumo-lamadi*, *cancer bush, kankerbos, kankerbossie*)[37] is a member of the Fabacea family. It has been used in humans in the treatment of cancer, tuberculosis, diabetes, chronic fatigue syndrome, influenza, rheumatoid arthritis, osteoarthritis, clinical depression and HIV infection. It has been reported that African Potato (common names: *magic muthi, yellow star, star lily*, *African potato, sterretjie, Afrika-patat*) is currently been used in some primary health care communities as an immunostimulant for patients with HIV/AIDS.[37]

The findings by Mills *et al.* (2005) have identified potential clinically significant drug interactions for both Sutherlandia and African Potato (*Hypoxis*) showing in-vitro inhibition of CYP3A4 and P-glycoprotein expression. Further in-vitro studies have also demonstrated the propensity for activation of Pregnane X Receptor (PXR), a nuclear receptor that controls the activation of both CYP3A4 and P-glycoprotein. These findings suggest that the co-administration of these herbal medicines with antiretroviral agents may result in the early inhibition of drug metabolism and

transport followed by the induction of decreased drug exposure with more prolonged therapy.[38]

1.4.3 Garlic *(Allium sativum)*

Hypercholesterolaemia is a common side effect of ARV treatment and garlic supplements are often taken to reduce cholesterol. The main active ingredient in garlic, which is known as allicin, has anti-parasitic and antibiotic properties [39] when used for gut problems. Severe gastrointestinal side effects have been reported with the simultaneous use of Ritonavir and garlic supplements.[34] Piscitelli *et al.* found that garlic supplements reduced the concentration of Saquinavir by more than 50%.[40] Saquinavir concentrations did not return to baseline after the 10-day washout period. The cause of prolonged depression in serum concentrations is unknown but may be related to a metabolite or component with a long half-life and enzyme-inducing capabilities.[40] It is recommended that patients should use caution when combining garlic supplements with Saquinavir when used as a sole PI.[40]

1.4.4 Milk-thistle *(Silybum marianum)*

Milk-thistle *(Silybum marianum)* is an herbal remedy commonly taken by HIV – infected people for the treatment or prevention of liver disease caused by hepatitis and the hepatotoxicicity of HIV drugs.[41] Milk-thistle is taken by many people co-infected with hepatitis C or who have HIV-related drug-induced liver problems. In fact some research [39] has hinted at its positive effect on liver health.[35] A study conducted on 10 healthy volunteers in the US concluded that the co-administration of Milk thistle and Indinavir had no apparent effect on Indinavir plasma concentration levels.[42] Furthermore, a study conducted by Mills *et al*. (2005) on 16 healthy volunteers in

Canada found that Indinavir levels were not significantly increased in the presence of milk thistle.[43] Research has shown that milk thistle should not interfere with Indinavir therapy in patients infected with HIV.[41]

1.4.5 Echinacea

Two well-designed studies evaluated Echinacea's effectiveness in upper respiratory tract infections in the general population. In one study, Echinacea reduced the duration of colds and the severity of the symptoms and in the other study Echinacea reduced the frequency and number of recurrences.[31] However, Echinacea may interact with drugs that can cause liver damage, thereby increasing the risk of liver impairment. Echinacea may also negate the effects of immuno suppressants, which are often used to prevent rejection of organ transplants. Echinacea causes inhibition of Cytochrome P450, family 1, subfamily A, polypeptide 2 (CYP1A2) and intestinal Cytochrome P450, family 3, subfamily A (CYP3A) activity and induction of hepatic CYP3A activity.[36] In patients on PIs, this may result in an increase drug levels in the blood. Clinicians recommend that people with Type 1 Diabetes, autoimmune diseases i.e. rheumatoid arthritis and multiple sclerosis, or diseases of the immune system (i.e. impaired by HIV/AIDS or Tuberculosis) should consult their doctor before taking Echinacea.[32]

1.4.6 Micronutrient use in HIV

The benefits of vitamin and mineral supplementation in HIV infection remain controversial. It has been shown that a healthy well-balanced diet is sufficient to meet the recommended intake for vitamin and mineral requirements.[44] Large doses of some vitamins and minerals can cause unpleasant side effects (e.g. vomiting,

abdominal cramping, diarrhoea) and can even be toxic (Table 1.2). [33, 36] In patients who are not taking ARV's there is evidence that supplementation can slow the progression of disease, possibly by redressing the alteration of vitamin and mineral levels caused by chronic infection. Between April 1995 and August 2003, 1078 HIV infected pregnant women in Dar es Salaam, Tanzania were recruited to examine the effect of daily supplements of vitamin A (in the form of vitamin A and beta carotene), multivitamins (vitamins B, C, E and folic acid), multivitamins plus vitamin A or placebo on the progression of HIV disease.[2] Women who received multivitamins had significantly higher CD4+, CDS+ and CD8+ cell counts and lower viral loads compared to the placebo group. In addition to enhancing immunity, multivitamins may also reduce viral replication, as indicated by the reduction in viral load. This study concluded that multivitamin supplementation delay the progression of HIV disease - thus delaying the initiation of ARV treatment in HIV infected women.[2]

Whilst the result suggests that nutritional status may affect the course of HIV disease, it is not known whether vitamin supplements delay HIV disease progression among people with superior nutritional status compared with participants in the study.[45]

A study conducted in Thailand found that supplementation with a wide spectrum micronutrient tablet was associated with a reduced risk of death in people with advanced HIV disease. Although supplementation had no significant effect on CD4+ cell count, plasma viral load or clinical disease progression, people with CD4+ counts between 101 and 200 cells/mm^3 who received the supplement in this placebo-controlled study were 67% less likely to die during the 48 weeks study. People with CD4+ cell counts less than 100 cells/mm^3 who received the supplement were 75%

less likely to die. No impact was seen, however, at CD4+ counts above 200 cells/mm^3. Supplementation was also not found to affect the risk of hospital admissions.[46]

Fawzi *et al.* (2006) also examined the effect of vitamin supplementation on quality of life and the risk of elevated depressive symptoms on 1078 HIV-positive women in Dar es Salaam, Tanzania.[47] They concluded that multivitamin supplementation (B-complex, C and E) resulted in a reduction in risk of elevated depressive symptoms comparable to major depressive disorder and an improvement in quality of life. However, Vitamin A did not have the same impact.

In patients taking ARV treatment, a broad-spectrum micronutrient formula developed by a Californian HIV practitioner has been shown to significantly increase CD4 cell counts by 25% over 12 weeks when used as an adjunct therapy to ARV treatment. The micronutrient was tested in a randomised and placebo-controlled study involving 40 HIV-infected people with peripheral neuropathy. The specially designed micronutrient combined 15 minerals, 15 vitamins and the anti-oxidants alpha lipoic acid, N-acetyl cysteine (NAC) and acetyl L-carnitine. Neuropathy scores improved by 42% in the micronutrient group compared to 33% improvement in the placebo group. However, the difference did not reach statistical significance. The conclusion was that micronutrient supplementation can significantly contribute to CD4+ cell count reconstitution in HIV-infected patients taking ARVs.[48]

In spite of this a recent editorial has called for more research into the benefits and limitations of micronutrient supplementation, both in patients taking ARV treatment and those that do not. There is also uncertainty surrounding the benefits of vitamins

and minerals in reducing oxidative stress and bone loss, and their effects in patients co-infected with tuberculosis or hepatitis B or C.[1]

Table 1.2: Toxicity of some vitamins and minerals commonly used in HIV.[33, 36]

Dietary supplement	Toxicity	Caution with ARV
Vitamin A	Doses above 9mg for men or 7.5mg for women may be harmful. Large amounts can cause liver and bone damage, vomiting and headache. Pregnant women should not take supplements containing vitamin A before consulting their doctors as high intakes may harm the unborn child.	None known
Vitamin C	Doses above 1000mg per day .May lead to kidney stones	Special care is needed if taking Indinavir (*Crixivan*).
Vitamin E	Doses above 800mg per day Associated with adverse effects; special care is needed if patients are taking anti-coagulants or have haemophilia.	Agenerase capsules contain vitamin E (36 IU/50 mg capsule), therefore additional vitamin E supplementation is not recommended. Formulations of Amprenavir (PI) provide high daily doses of vitamin E. Adult and paediatric patients should be advised not to take supplemental vitamin E since the vitamin E content of Amprenavir capsules and oral solution exceeds the Reference Daily Intake (adults 30 IU, paediatrics approximately 10 IU)
Vitamin B_6	More than 2g per day associated with nerve damage, but even doses as low as 50mg per day have been associated with peripheral sensory neuropathy	None known
Zinc	More than 75mg per day have been linked with copper deficiency, a shortage of neutrophils, and anaemia.	None known
Selenium	More than 750µg per day are associated with immune suppression	None known

1.5 Choosing CAM Therapies

Many HIV-infected people are exploring CAM therapy as a means to relieve HIV-related symptoms and, in some cases, to inhibit viral activity.[7,49] The more symptomatic the patient, due to disease progression or drug side effects, the more likely the patient is to supplement with CAM.[50] The opportunity to manage certain symptoms of the HIV disease may not only improve patient wellbeing but also influence immune status and integrity in this population.[26] In a clinical trial among 100 HIV-infected patients in the US, the most commonly reported reasons for CAM therapy use was: nausea, insomnia, dermatological problems, weakness and depression.[51] Moreover, a study performed on 180 HIV-infected patients attending a general medical practice, symptoms such as weight loss, nausea, and diarrhoea prompted many of the patients to try herbs, vitamins and supplements for symptom relief.[8] Primary reasons according to Calabrese *et al*. (1998) for seeking CAM therapies such as acupuncture and massage were pain, depression and stress.[52] Current research suggests that HIV-infected patients are turning to CAM therapy in the hope of reducing symptoms associated with HIV/AIDS, managing the side effects of drug therapy, maximising quality of life, slowing disease progression, as a way to better cope with their illness.[28,47,53] Most people living with HIV/AIDS (PLWHA) in the UK do not choose CAM as an alternative to ARV treatment, but use CAM to complement ARV treatment.[29]

1.6 Socio-economic and Demographic Influences

Research suggests that CAM therapy use is more likely among women, MSM [52], young and educated PLWHA.[8,51] In earlier research Tsao *et al.* (2005) found that patients with high school or less education (relative to a bachelor's degree or more)

was less likely to use CAM therapies. Moreover, patients with CD4+ counts below 500 were likely to use *fewer* CAM therapies than those with CD4+ counts of 500 or more.

More current research[56] indicates that sexual orientation and socio-economic class also impact on CAM use: MSM from middle-class backgrounds are more likely to have used complementary therapies. Non-Caucasian MSM with HIV/AIDS viewed complementary therapies as an aspect of their cultural heritage, whereas intravenous drug users situated their use of CAM therapies to health care in relation to issues concerning addiction and rehabilitation.[56]

1.7 Where do HIV Infected Individuals Gather Information about CAM Therapies

Sources to gather information on CAM therapies are varied but include CAM providers (Alternative health practitioners), physicians, books, resources from AIDS Service Organizations, the internet and health food stores.[57] According to De Visser *et al.* (2002) PLWHA appear to be more involved in the HIV/AIDS community – they are more likely to read HIV/AIDS magazines/newspapers, and spent more free time with other PLWHA.[29]

1.8 Disclosure of CAM Therapy Use

Despite the potential risks of CAM therapy, there is evidence that physician – patient disclosure and dialogue about CAM therapy use is infrequent.[6,31] A study on US adult patients found that 72% of patients did not inform their physician about their CAM use.[7] These patients had symptoms that ranged from diarrhoea, nausea and vomiting and hypertension. As a consequence the physician prescribed allopathic treatments without knowing the full context of their patients' symptoms. Without knowing about a

patient's use of CAM therapies, the allopathic physician has little basis for understanding fluctuations in the patient's condition.[57]

1.9 Purpose of this Study

Studies have shown that the use of CAM therapies among adult HIV-infected patients is on the increase worldwide.[6, 7] Healthcare professionals in developing countries are more used to patients using CAM therapy, however in the UK, this is still relatively new and many health professionals are not familiar with these products. Limited evidence is available in the UK regarding the safe and effective use of CAM in the treatment of HIV/AIDS and its complications. The main purpose of this study was to establish the prevalence of CAM therapy use among adult HIV-infected patients attending an outpatient clinic at Whipps Cross University Hospital, London, UK. Additionally this study was also aimed at exploring reasons for CAM therapy use, factors that would impact on the decision to consume CAM therapies and the fiscal burden of CAM therapies on an individual with HIV.

The results of the study would be used to educate local healthcare professionals in the use of CAM therapy, in the light of the previously mentioned potential drug-herb interactions.

CHAPTER 2: METHODOLOGY

2.1 Aim

The aim of this research project was to determine the prevalence of CAM therapy use amongst adult HIV infected patients in an outpatient clinic at Whipps Cross University Hospital, London, UK.

2.2 Objectives

To determine the following specific objectives:

1. Reasons for using CAM therapies and monthly expenditure with CAM therapies.
2. Resources for information about CAM therapies.
3. Disclosure of CAM therapy use to a doctor or other health care professional.
4. Knowledge regarding interactions between antiretroviral therapy and CAM therapies.

2.3 Null-Hypothesis

Complementary and alternative medicine is not used in people living with HIV/AIDS in the UK.

2.4 Study Design

A prospective, observational study was performed on patients diagnosed with HIV. The study was conducted between July 2005 and November 2005 in the Department of Sexual Health (DOSH), Whipps Cross University Hospital, London, UK

2.5 Study Population

The study population attending the DOSH came from the London Borough of Waltham Forest in East London, England and forms part of Outer London consortium (Appendix 1). Out of the 376 local government districts in England and Wales, Waltham Forest has the 11th largest non-white minority ethnic population. The largest minority ethnic group are black Afro-Caribbeans/Africans with a population of 30,300, followed by Pakistanis who number over 17,000. Out of the 376 local government districts in England and Wales, it ranks 19th for over-crowded housing conditions, 29th for unemployment and 17th for number of single-parent households.

The total numbers of patients with diagnosed HIV infection in DOSH, Whipps Cross Hospital (Waltham Forest), in 2004 was 561 and for North East London 4031 (Table 2.1). More recent data is not available on this area.[60]

Table 2.1: Diagnosed HIV prevalence by age group in 2004

	England	**London**	**Waltham Forest**
	2004	**2004**	**2004**
Age (years)	**N**	**N**	**N**
0 - 14	1310	714	27
15 - 24	1677	754	21
25 - 39	19778	10294	289
40 - 54	13425	7654	200
55+	2579	1258	24
All ages	**38769**	**20675**	**561**

Source: Survey of Prevalent HIV Infections Diagnosed (SOPHID), 2005

The reason for choosing this population and area for the research project was related to the investigator being based at this DOSH clinic.

2.6 Sampling Method

The sampling method used was convenience sampling. Patients were approached by the investigator at DOSH, between July 2005 and November 2005 and asked to participate in this study**.** All patients attending the outpatient clinic that were already diagnosed with HIV regardless of gender and ethnicity, between the ages of 18-60 were eligible for inclusion in the study. Patients that did not speak English were also included, as there was a translation service available to the DOSH. Patients were only excluded if they were aged 61 years and older (as there were no HIV positive patients older than 60 registered in the clinic) less than 18 years, or inpatients in the hospital. Patients that were not willing to participate were not included in the study. The use of CAM therapy was established once the patient was enrolled in the study and this data was used for further analysis.

The number of patients in this study was dependant on the attendance of patients during the period as well as consent obtained from the subjects. The investigator was aiming to recruit 100 patients out of the 561 patients currently diagnosed with HIV in this DOSH at Whipps Cross Hospital.

2.7 Questionnaire Development

The questionnaire (Appendix 4) for self-administration was developed by reviewing the last 2 years dietetic records for the most commonly used CAM therapy in the area. In addition an extensive literature search was performed; using only reputable peer reviewed resources. Although a plethora of information is available in the lay press on CAM therapy, these resources were deemed not suitable for this study, due

to the lack of evidence base and peer review. The Pubmed database was searched for relevant literature. Searches were limited to English language only.

The following terms were used: “HIV/AIDS, CAM therapies”, “herbal remedies, African traditional remedies”, “drug interactions, herbal remedies, antiretroviral treatment”, “HIV, complementary therapies”, “St. John’s Wort, antiretroviral medication, drug interactions”. Following the literature search the investigator reviewed all available studies and excluded those that were not related to the study. The content validity of the questionnaire was therefore based on the available literature.

After consultation with the Research and Development Team at Whipps Cross Hospital regarding questionnaire development, advice was given to keep questionnaires as short as possible to increase patient participation. This advice was based on previous studies conducted at DOSH.

The questionnaire consisted of 4 sections (Table 2.2). All patients had to complete section A (2 questions) and section B (3 questions). The last 2 sections in the questionnaire were different: Section C (8 questions) was completed by patients not on HIV treatment and Section D (10 questions) was completed by patients on HIV treatment.

The 4 sections of the questionnaire were divided into the following: information about the respondent’s socio-demographical status, HIV status, ARV treatment naivety and ARV treatment experience. The questionnaire used a tick-box format, which were

converted to numeric values for data analyses. The coding system ensured that the information could be easily entered into a computer (Table 2.2).

To avoid confusion and ensure correct interpretation of questions, the questions were clearly worded in simple language, which could be understood by all respondents. Subsequently, face validity was tested in a pilot study questionnaire at Newham General Hospital, London on patients with a similar medical history to ensure face validity. The pilot study was conducted during May 2005 and 10 patients completed the questionnaire. The HIV centre at Newham General Hospital, where the pilot study was performed, provided an unbiased, but similar HIV population to the DOSH at Whipps Cross Hospital, as that the hospital was also within the East London Consortium. Feedback form the pilot study was positive and no changes were necessary. However the feedback from the local Research and Development Committee indicated that the questionnaire was too long (12 pages). Therefore the font size of the questionnaire was reduced from 12 font to 10 font, which reduced the number of pages of the questionnaire to 8 pages. The study population at the research centre was therefore not consulted to obtain face validity of the questionnaire.

In addition to socio-demographic data (age, gender, education level and employment status), respondents indicated the time frame since awareness of HIV positive status, their self-perceived state of current health and if they currently use ARV medication. Those using ARV medication indicated whether they experienced any side-effects taking ARV medication, time period since taking ARV treatment. All respondents were asked if they currently used CAM therapies and then had to indicate the types

of CAM therapies used, their monthly expenditure on CAM, reasons for using CAM therapies, sources of information on CAM, at what point CAM was initiated.

In line with the official CAM therapy classification, the questions on CAM therapy use were categorised into 3 groups (Figure 1.1):

- Herbal remedies
- Nutritional supplements/vitamins and
- Lifestyle/ homeopathy.

Participants also indicated whether they had consulted a doctor or other health care professional before CAM usage and if they were aware of any herb-drug interactions. Some participants indicated the use of CAM therapies from multiple categories.

Table 2.2: Questionnaire description

Sections	Description	Content
A	Socio-demographic information	Education level Employment status
B	HIV status	Time frame since awareness of HIV status Patients' current state of health (self- perceived) Use of HIV medication
C	ARV treatment naïve patients	Complementary and alternative therapies categorised under herbal remedies, nutritional supplements/vitamins and lifestyle/homeopathy At what point in time CAM was initiated Reasons for using complementary and alternative therapies (CAM) Sources of information on CAM
D	ARV treatment experienced patients	Time frame of anti-HIV treatment usage Symptoms experienced Complementary and alternative therapies categorised under herbal remedies, nutritional supplements/vitamins and lifestyle/homeopathy At what point in time was CAM initiated Reasons for CAM usage Sources of information on CAM Monthly expenses concerning CAM Were health care professionals consulted before CAM usage Awareness concerning herb-drug interactions

2.8 Data Collection

An information sheet (Appendix 2) explaining the purpose of the study was issued to all potential participants by the investigator when they attended the clinic for their viral load and CD4+ count testing (clinic attendance 1) between July 2005 and November 2005 (Figure 2.1). Patients had 2 weeks to consider whether or not to participate in the research project. As per clinic procedure, patients normally attend their consultant appointment after 2 weeks from the date they had their viral load and CD4 count testing. Patients then indicated to the investigator that they wanted to

participate in the project. The investigator was available four days of the week in the DOSH. Figure 2.1 gives and schematic outline of the process of data collection for this project.

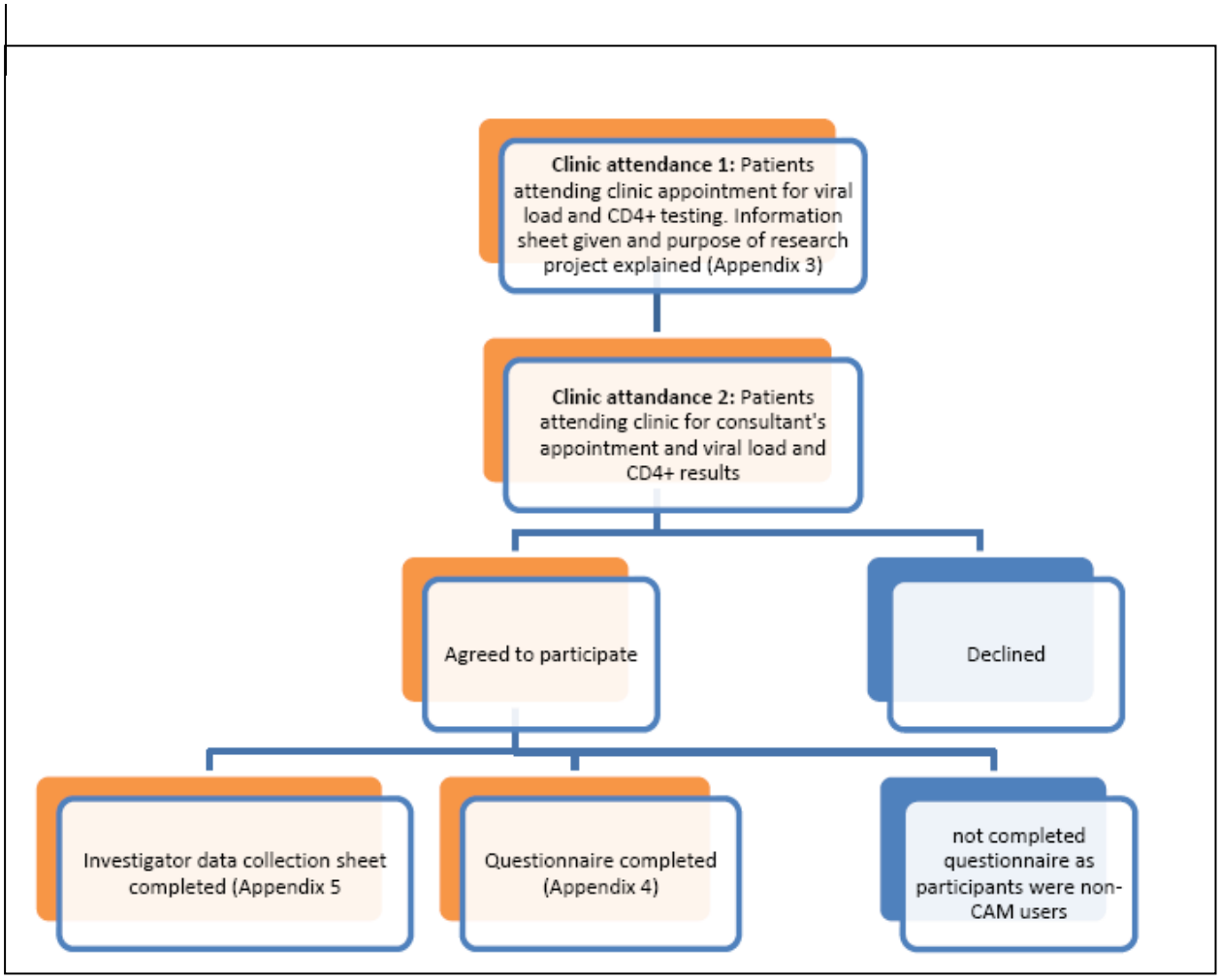

Figure 2.1: Flow chart of data collection

Participants were given a guarantee that all responses in the questionnaire would be kept anonymous and confidential (as indicated in the information sheet) and that participation in the project would not prolong their waiting time to see the clinic consultant. Participants did not have to sign a consent form as this project was regarded as an audit, which formed part of the current clinical practices (UK Ethics Committee policy). The completion of the questionnaire was accepted as signed

consent. In order to ensure confidentiality, each participant received a reference number that was used on all documentation. The questionnaire (Appendix 4) was then given for self-completion in a private clinic room, whilst attending the clinic. On completion, participants placed the questionnaire in the return box for completed questionnaires which was located at the clinic's receptionist desk. The Investigator data Collection form (Appendix 5) was then completed by the investigator for each participant in the study with correlated reference numbers.

Subjects were offered the support of a translation service which was available from Waltham Forest Interpretation Service from the London Borough of Waltham Forest Council. Participants who required translation could do so through the Patient Advisory and Liaison Service (PALS). All interpreters were trained to translate medical information and the investigator spent time with the interpreter to explain the purpose of the study and questionnaire.

2.9 Data Analysis

A statistician appointed by the Faculty of Health Science, University of Stellenbosch, analysed the data. Statistica 7.1, SAS and SPSS 14 were used for all statistical analysis.

Descriptive data of the subjects was presented as mean, median and standard deviations (SD) and the frequency and type of CAM therapy was presented in percentages. Cross-tabulation was used to determine prevalence and reasons of CAM use and expenses. The maximum likelihood chi-square test for nominal data

was used to establish whether CAM therapy use was related or due to gender, race, and education.

Data checking and screening took place before formal data analysis by the investigator. Data was excluded from formal data analysis if the questionnaire was incomplete.

2.10 Ethics Approval and other Considerations

Ethics approval was obtained from the Human Research Committee of Stellenbosch University (Ethics Reference Code N05/07/108). The NHS did not require Research and Ethics Committee approval as this project was regarded as an audit, which forms part of the current clinical practices. Therefore no written consent was required for this study. All information that was collected during the course of the study was kept confidential. Anonymous data was stored on a personal computer, which was password protected. Completed questionnaires were kept in a locked filling cabinet at the DOSH.

CHAPTER 3: RESULTS

3.1 Sample Description

There were 561 HIV positive patients registered at the DOSH, Whipps Cross Hospital in 2004. All patients that attended the Whipps Cross Hospital HIV Clinic (DOSH) during July 2005 and November 2005 (*N* = 367) were given the opportunity to participate. Only 112 patients were prepared to take the time to read through the patient information sheet. From these 112 patients, 81 patients (72% of total) agreed to participate and therefore received a questionnaire. The main reasons for not participating in the study were issues related to confidentiality and time constraints as documented in the medical notes by the clinic consultant. Thirty eight participants (47%) of the 81 patients indicated that they had never used CAM therapies and therefore did not complete the questionnaire. Thus, a total of 43 (53%) of the 81 patients had used CAM therapy and completed the questionnaire. However 9 (21%) of the 43 questionnaires were incomplete and could not be included in data analysis. Missing data included incomplete reference numbers as allocated by the investigator, and socio-demographic information. Therefore, only 34 (79% from 43 questionnaires) remained eligible for data analysis **(**Figure 3.1). None of the 34 study participants required the translator services.

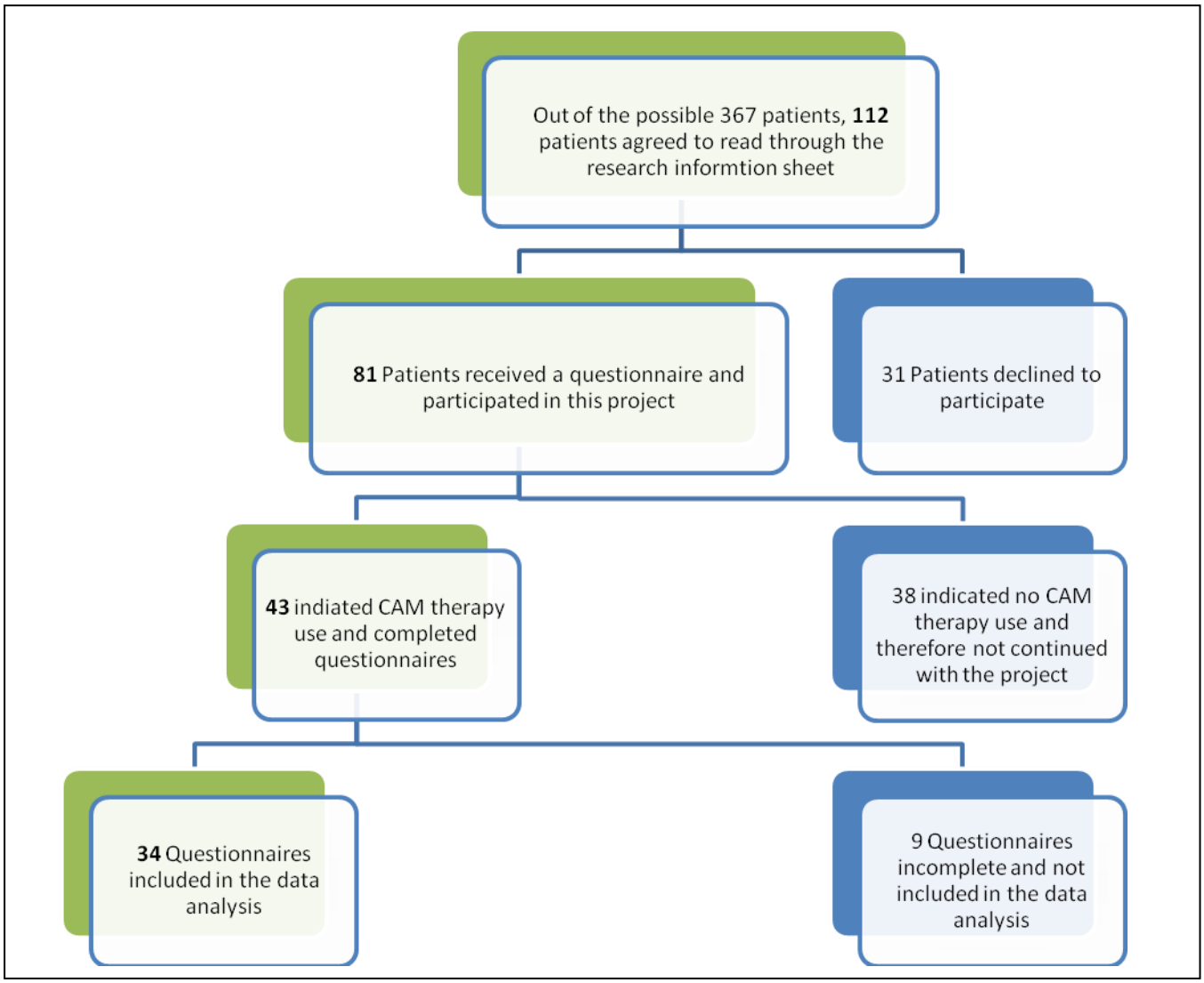

Figure 3.1: Schematic outline of completed questionnaire

The investigator data collection sheet was used to collect the demographic information of the study participants i.e. gender, age and ethnic origin. As well as the demographic information, the investigator data collection sheet was used to establish how many of the study participants was using ARV treatment or not.

The patients included in the study (*N*= 34) consisted of 10 women (29%) and 24 men (71%). The average age was 39.5 (age range 28 to 61 years; Standard Deviation (SD) 8.614) (Table 3.1).

Demographic analysis indicated that 17 subjects (50%) were Caucasian and represented a range of ethnic backgrounds, including British, Irish and French. Another 16 subjects described their ethnicity as Black (47%) (African or Caribbean descent) and 1 subject describe his ethnic origin as Chinese (Table 3.1).

Educational level included patients with Secondary/High School (*N* = 5), College (*N* = 13), University Degree (*N* = 10) and Post Graduate Education (*N* = 6) (Table 3.1). No significant difference between patients' use of CAM therapies and educational level was found (p = 0.17).

From the total sample (*N* = 34) 15 participants (44%) were unemployed (Table 3.1).

Table 3.1.Demographic description of the sample

		N = 34	%
Gender	Male	24	71
	Female	10	29
Ethnic origin	Caucasian	17	50
	Black African	15	44
	Black Caribbean	1	3
	Other	1	3
Age	Mean age of patients in years	39.5 years	
	Standard Deviation	8.614	
	Age range	28 – 61 years	
Using ARV	Yes	26	**76**
	No	8	24
Education	Secondary/High School	5	15
	College	13	38
	University	10	29
	Post Grad Education	6	18
Employment	Full time paid employment	8	24
	Part time employment	4	12
	Self employed/freelance	4	12
	Unemployed	15	**44**
	Student	3	9

Of the 34 questionnaires that remained eligible for data analysis, 26 (76%) participants were on ARV treatment. The remaining 8 (24%) were ARV treatment naïve. Using the Chi-square test to compare the ARV group (*N* = 26) and the non – ARV group (N = 8), there was a statistical difference between the two groups (p = 0.002) for ethnicity (p = 0.000) and gender (p = 0.002) (Table 3.2). However, there

was no statistical difference between the ARV group and non-ARV group in terms of age.

Table 3.2 Test Statistics for age, gender and ethnicity

	Difference between ARV and non-ARV Group	Age	Gender	Ethnicity
Chi-Square	9.529	5.118	5.765	29.529
df	1	18	1	4
Asymp. Sig.	.002	.999	.016	.000

Twenty three (67%) of the participants in this study (*N* = 34) have been living with HIV for 5 years or less. The remaining 11 participants (33%) of the sample (*N* = 34) indicated that they have been living with their HIV diagnosis for more than 5 years.

In response to the question regarding current state of health, 18 subjects (53%) of the total sample (*N* = 34) described their health status as good, 18% (*N* = 6) indicated their health status as fair, 34% (*N* = 5) chosen excellent, 12% (*N* = 4) as poor and the remaining 3% (*N* = 1) indicated health status as very poor.

3.2 Study Outcomes in terms of Objectives

3.2.1 Prevalence of CAM therapy use

From the 81 patients that agreed to take part in study, 34 patients (53%) used CAM, and 47% did not used CAM therapy. Fifteen subjects (44%) indicated that they took garlic, 27% (*N* = 9) took Ginseng, 27% (*N* = 9) took Echinacea (Table 3.3). Other herbal remedies consumed included Chinese Medicine (18%, *N* = 6), St. John's Wort (18%, *N* = 6) and Avurvedic medicine (15%; *N* = 5). Twenty four subjects (71%) reported that they took a multivitamin/mineral, 41% (*N* = 14) took vitamin E, 38% (*N* = 13) took selenium, 12% (*N* = 4) took glutamine and 18% (*N* = 6) reported 'other

nutritional supplement/therapies' use. Other CAM therapies included Ginko Biloba (*N* = 1), cod liver oil (*N* = 1), recreational drugs (Cocaine, Crystal Meth) (*N* = 1), physiotherapy (*N* = 1), Milk Thistle (*N* = 1), reflexology (*N* = 2), dehydroepiandrosterone (DHEA) hormone (*N* = 1). CAM therapies used by fewer than 10% of participants included Tibetan Medicine, Sutherlandia, African Potato (Hypoxis) and chiropractic therapy.

In the Lifestyle/homeopathy section, 50% (*N* = 17) indicated that they exercised regularly, 32% (*N* = 11) had regular massages, 24% (*N* = 8) prayed regularly, 24% (*N* = 8) had regular acupuncture. Meditation/visualization and Reiki was practised by 15% (*N* = 5) respectively. Yoga was practised by 12% (*N* = 4).

All of the participants indicated the use of CAM therapies from multiple categories. Statistical analyses using the maximum likelihood chi-square test compared CAM use of the ARV treatment group (*N* = 26) to the non – ARV treatment group (*N* = 8). No statistically significant difference (p = 0.57) between the two groups was found. Nineteen (73%;*N* = 19) participants who were taking ARV treatment started CAM therapy after diagnosis and the remainder commenced CAM prior to diagnosis. Five (63%) participants from the non-ARV group started CAM prior to diagnosis and the remainder commenced CAM after HIV positive diagnosis.

Table 3.3: Most commonly used CAM therapies

CAM	N (%)
Herbal remedies	
Garlic	15 (44)
Ginseng	9 (27)
Echinacea	9 (27)
Chinese medicine	6 (18)
St. John's Wort	6 (18)
Ayurvedic medicine	5 (15)
Other	4 (12)
Sutherlandia	2 (6)
African Potato (Hypoxis)	2 (6)
Tibetan medicine	0 (0)
Nutritional Supplements/Vitamins	
Multivitamin/mineral supplements	24 (71)
Vitamin E	14 (41)
Selenium	13 (38)
Other	6 (18)
Glutamin	4 (12)
Lifestyle/Homeopathy	
Exercise	17 (50)
Massage	11 (32)
Prayer/Faith healing	8 (24)
Acupuncture	8 (24)
Meditation/visualization	5 (15)
Reiki	5 (15)
Yoga	4 (12)
Other	4 (12)
Chiropractic therapies	1 (3)

*Combinations of CAM therapies excluded; all patients used multiple CAM therapies

Twenty nine participants (85%) did not believe that CAM therapies cured HIV/AIDS. Only 5 participants (15%) indicated that they believed that CAM therapies did indeed cure HIV/AIDS.

3.2.2 Reasons for using CAM therapies and monthly expenditure with CAM therapies

Of the total sample of patients using CAM therapy (*N*= 34), 79% (*N*= 27) thought that CAM therapies improved their general health and ensured long term survival, 9% (*N* = 3) recorded that CAM therapies gave them more control over their health, 3% (*N* = 1) of the subjects indicated dissatisfaction with conventional medication, 3% (*N* = 1) used them due to family tradition/culture, 3% (*N* = 1) thought CAM therapies reduced the side-effects of conventional medication and 3% (*N* = 1) gave 'other reasons' for CAM therapy use (Figure 3.2).

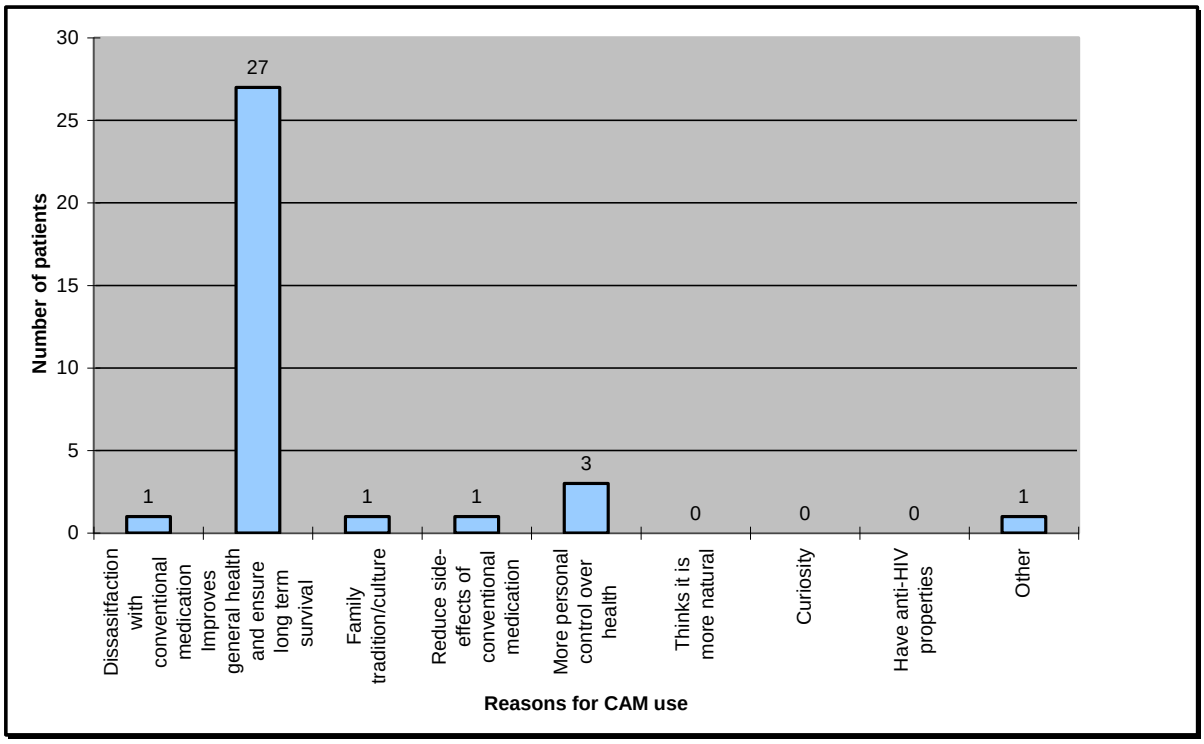

Figure 3.2: Reasons for CAM therapy use

Statistical analysis using the maximum likelihood chi – square test comparing pooled reasons for CAM therapy use between the ARV treatment group (*N* = 26) and the non – ARV treatment group found no significant (p = 0.13) difference. However, 81% (*N* = 21) of participants in the ARV treatment group (*N* = 26) indicated their main reason for CAM therapy use was that it improves their general health.

Twenty one (62%) of the 34 CAM users spent on average ≤ £10 per month on CAM therapies, 12% (*N* = 4) spent between £11 and £20, 15% (*N* = 5) spent on average £21 - £30, 6% (*N* = 2) spent between £31 - £40, 3% (N = 1) indicated spending between £41 - £50 and 3% (N = 1) spent ≥ £50. Statistical analysis using the Chi-square test between the ARV treatment group (*N* = 26) and the non- ARV treatment group (*N* = 8) in terms of monthly expenditure was not significant (p = 0.62). From the total sample of 34 subjects, 44% (*N* = 15) were unemployed. 80% (*N* = 12) of these 44% unemployed subjects indicated that they spent on average ≤ £10 per month on CAM therapies, 15% (*N* = 2) spent between £21 - £30 and 7% (*N* = 1) spent on average £11 - £20.

3.2.3 Sources of information about CAM therapies

Thirty two percent of participants reported receiving information about CAM therapies from health care professionals (doctors, nurses, and dietitians), 12% from Traditional Healers, health food stores and internet/articles/newspapers respectively. A further 9% received information from other non-positive HIV friends/relatives, 6% from alternative therapist, HIV positive friend and HIV/AIDS organizations respectively and 6% indicated ‘other’ as a source of information about CAM therapies.

The Chi-square statistical test was used to indicate whether ARV treatment and non-treatment groups' sources of information differed significantly. The results indicated that there was no difference between the ARV treatment group (*N* = 26) and the non-ARV treatment group (*N* = 8) in obtaining information on CAM therapy (p = 0.63).

3.2.4 Disclosure of CAM therapy use

Subjects were asked whether they disclosed the use of CAM therapy to their doctor or primary care provider. Seventy three percent (*N* = 25) of participants reported not discussing CAM therapy use with their doctor or primary care provider. Statistical analysis (Chi-square test) between the ARV treatment group (*N* = 26) and non – ARV treatment group (*N* = 8) showed no difference between the 2 groups (p = 0.43).

3.2.5 Knowledge regarding antiretroviral treatment and CAM therapy drug - herb interactions

Eighteen (53%) of the participants were aware of possible ARV drug interactions with CAM therapies especially herbal remedies. Statistical analysis using the Chi-square test, compared the knowledge of ARV drug - herb interactions between the ARV treatment group *(N* = 26) and the non- ARV treatment group (*N* = 8). The results might indicate that patients in the ARV treatment group had more awareness than the non – ARV treatment group (p = 0.006).

CHAPTER 4: DISCUSSION

The main purpose of this research project was to determine CAM therapy use amongst adult HIV infected patients in an outpatient setting. The research project also set out to identify why patients with HIV access these therapies, monthly expenditure on these CAM therapies, sources of information regarding CAM, disclosure to their primary health care provider and knowledge regarding possible drug interactions between ARV's and herbal remedies. A total of 81 patients were included in the study, of which thirty-four patient questionnaires of CAM users could be assessed for statistical purposes.

4.1 CAM Therapy Use

The prevalence of CAM therapy use in this population was 53%, therefore rejecting the null hypothesis. In this study the majority of patients (85%) did not think that CAM therapy cured HIV. Rather, CAM therapies were used to complement ARV treatment. The high prevalence of CAM therapy use in conjunction with ARV treatment in our study highlights the urgent need for doctors and health care professionals (and all the other potential resources where patients get CAM information) to understand the health benefits and risks of using CAM therapies along with ARV treatment in people living with HIV/AIDS.

In line with previous studies, multivitamins and minerals were most commonly used as CAM therapy in CAM users. Previous research by Gore-Felton *et al.* indicated that mega-doses of vitamins are not uncommon amongst HIV-positive patients [55, 49], however the efficacy and safety of such a practice amongst this population is still unknown. A study by Fawsi *et al.* (2004) indicated that a multivitamin supplementation delayed the progression of HIV disease.[47] It can also provide an alternative and effective low-cost means of delaying the start of ARV treatment in HIV

–positive women in resource poor settings. Another study [46] found that micronutrient supplementation can significantly improve CD4 cell count in HIV-positive patients taking ARV treatment. The micronutrient tested was well tolerated by the patients and it has been suggested that micronutrients could be used as an adjuvant to ARV treatment. More research, however, is warranted and patients should be informed of the risks of mega-doses of micronutrients in terms of toxicity and interactions with ARV treatment.

In our study, garlic was used by 44% of the study participants. As was mentioned earlier in chapter 1, severe gastrointestinal side effects have been reported with the simultaneous use of Ritonavir and garlic supplements.[34] Piscitelli *et al.* found that garlic supplements reduced the concentration of Saquinavir by more than 50%.[40] It has been recommended that patients should use caution when combining garlic supplements with Saquinavir when used as a sole PI.[40]

Results from this study indicated that 27% of the participants used Echinacea. The use of Echinacea for people with HIV remains controversial. There is no known published research to document any dangerous results from the use of Echinacea by people with HIV. However, further study is needed as in vitro studies have shown in increase in tumor necrosis factor, which could worsen HIV infection.

St. John's Wort was used by 6 participants (18%) in this study. Considering the well documented drug-herb interactions between St. John's Wort and Indinaivir and nevirapine respectively, patients should be advised to avoid co-administration of these two herbal therapies with St. John's Wort. Co-administration may result in suboptimal antiretroviral drug concentrations, leading to loss of virologic failure and development of resistance or class cross-resistance. [35, 36]

Only 2 participants in this study indicated that they've used Sutherlandia and another 2 subjects used African potato. Investigators have identified the potential for clinically significant antiretroviral drug interactions as both Sutherlandia and African potato inhibited CYP3A4 and P-glycoprotein expression in-vitro. Caution should be taken when introducing these herbal drugs into the routine care of HIV positive people[38,39].

4.2 Reasons for CAM Therapy use and Monthly Expenditure

In our study, we found that for many people living with HIV/AIDS the most important reason for using CAM therapy is the belief that CAM improves their general health and ensures long-term survival. In contrast a previous study [29] found that CAM therapies are used to reduce and manage the side effects of ARV treatment. A study in the US [30] found that many people living with HIV/AIDS used CAM therapies because they believed that CAM therapies can reduce the symptoms of HIV infection and side-effects of the ARV treatment. In our study only 3% (*N* = 1) indicated that CAM therapy use was associated with reduction of ARV treatments side effects. Studies amongst adults with chronic diseases such as cancer, arthritis, cardiovascular disease, diabetes and lung disease, indicate that adults with diagnosed chronic diseases are more likely to use CAM therapies compared to adults with none of the reported chronic diseases.[56] As the majority of HIV-infected outpatients in this study are CAM users, it can be concluded that HIV-infected patients display similar tendencies as patients with other chronic diseases.

Other potential reasons for the use of CAM therapies, included fighting HIV or boosting immunity, relieving stress or depression, improving memory or concentration and increased weight gain were not included in this questionnaire, on recommendation from the Research and Development committee at Whipps Cross

Hospital. The committee thought that the inclusion of all these factors would make it too long and cumbersome for the patients and can be seen as a limitation of this study. These factors were also not mentioned in question 8 of section C and D of questionnaire named 'other'. However, these do require further research.

Interestingly this project has found that the study subjects spent an average of <£10 a month on CAM therapies. Persons living below a certain income level may be less able or willing to buy CAM therapies. However we found that 44% of this study's participants were unemployed of which 80% spent on average < £10/month on CAM therapies. Weekly income support benefit in the UK is on average £59 per week. Spending an average of £10 on CAM therapy therefore disposes a significant amount of income. A study by Fairfield *et al.* (1998) indicated that CAM therapies were predominantly paid for out-of-pocket and this burden might be substantial for low-income groups. From our study one can conclude that income and employment status did not predict CAM use. This is an interesting finding and should be further explored in future research.

4.3 Sources of Information regarding CAM

In our study most of the participants (32%) indicated that they received information regarding CAM from their doctor or other health care professionals. This is consistent with a study by Gore-Felton *et al*., who found that medical professionals were the most important information source regarding CAM therapies. In contrast with a study conducted by De Visser *et al.* (2000) which indicated that HIV–positive people received information from other PLWHA, HIV/AIDS magazines/newsletters and the HIV positive community. A major source of information in the HIV population is the Internet, HIV related TV and HIV magazines.[29] It is debatable whether access to

these resources are dependant on the HIV positive patient disclosing their status to family/friends Therefore one can hypothesis that our study participants who have not disclosed their status to families/friends for fear of isolation/stigma, also might not access these sources of information. Therefore, they might not play an active role in the HIV community or spent any time with other HIV-positive people. This, however, is highly speculative and further research is warranted.

4.4 Disclosure of CAM Therapy Use

Results of our study suggested that most of the participants (73%) did not disclose their CAM therapy use to their doctor or health care professional and 32% reported that their main source of information for CAM therapy came from health professionals. In the absence of published research, one can only hypothesise that this is related to a lack of knowledge from both healthcare providers and patients that CAM therapy can interfere with ARV treatment. Due to this, both parties might deem it unnecessary to mention or ask about its use. It is therefore important to address this lack of knowledge in primary health care providers working with HIV -patients. Given the large proportion of people living with HIV/AIDS, as well as the proportion of patients using CAM therapies, it is important that doctors and other health care professionals develop a greater awareness of the prevalence of use as well as possible drug interactions.

4.5 Knowledge Regarding Interactions between ARV's and Herbal Remedies

Most of the participants in our study were aware of possible drug interactions between ARV treatment and herbal remedies. There was a significant difference between HIV positive patients taking ARV treatment and ARV treatment-naïve

patients in terms of possible drug-herb interactions. One could speculate that due to patients taking ARV treatment they take a more active role in their health and treatment, and are therefore more aware of possible drug interactions. Currently, the protocol in DOSH requires that all HIV positive patients to start on ARV treatment have a consultation with both the HIV specialist pharmacist and Dietitian. Both the Dietitian and Pharmacist would question the patient about CAM therapy use. This may highlight the potential interactions to the patient taking ARV treatment, which may explain the significant difference in the knowledge between the ARV treatment group and the ARV treatment-naïve group.

4.6 Limitations of this Study

Our study has several limitations. Firstly, the convenience sampling method could be seen as a limitation. A convenience sample chooses the individuals that are easiest to reach. In this study, it meant that all patients that attended the clinic were eligible for the study. Convenience sampling does not represent the entire population so it is considered bias, therefore, if clinics were not attended, they would not have been approached to participate in the study. Thus, caution should be used when generalizing these findings to all people living with HIV/AIDS in the Borough of Waltham Forest where this study was conducted.

However, even with this limitation, the prevalence of CAM therapy use indicates that further clinical studies are needed to determine the long-term efficacy of CAM therapy use in conjunction with ARV drugs.

Another limitation was our choice of CAM therapies. Whilst our choice of CAM therapies included a multivitamin/mineral supplementation, vitamin E and Selenium,

we did not include other single vitamins and minerals such as iron, Vitamin B_{12}, folic acid or other that are often recommended or prescribed by medical doctors. The reason for not including specific micronutrients and dosages are related to the CAM therapy classification, which was used as the basis for the questionnaire. An indication of how many patients are taking micronutrient doses above the recommended dietary requirements could have been valuable in determining the risk of micronutrient toxicity in our population group.

The inclusion or exclusion of certain CAM therapies can change prevalence estimates. Our findings can therefore not be generalized to HIV positive patients in other boroughs of London and other counties in the UK, or to patients who did not participate in this study. In our study we made use of the universal definition for CAM use.

The limited number of herbal therapies included in this study might be interpreted as a limitation. However, the use of herbal therapies are not as common in the UK as in developing countries.[38] Therefore the questionnaire included only those herbal remedies most commonly used in the UK.

Our small sample size is also considered a limitation. The design for the study was chosen because of the number of participants for this study was dependant on clinic attendances during the study period as well as patients' consent to participate. Additionally, follow – up of well-controlled HIV patients only occurred once a year in the clinic where the study was performed. Despite these limitations the investigator recruited 112 patients out of a possible 367 patients in this clinic during the 5 month study period that was willing to read the study information sheet. The findings may certainly not be representative of patients in the UK, but does provide a good

indication of the level of CAM therapy use in the local Whipps Cross area and may be used as a pilot study for further research in this area.

There was a statistical difference between the ARV (*N* = 26) and non- ARV group (*N* = 8). This could be seen as a limitation of this study in terms of a higher prevalence of CAM use amongst HIV – infected individuals not on ARV treatment and those on ARV treatment. However, a study by Joseph *et al*. (2003) demonstrated similar rates of CAM use amongst ARV and non – ARV patients.[61]

Finally, the use of articles only in the English language may be seen as a limitation. However, only a few studies on the Pubmed website were published in other languages and the gross majority were in English. The investigator was also limited to the English language and did not have additional funding for the translation of articles.

CHAPTER 5: CONCLUSION

Complimentary and alternative medicine therapies can be defined as those therapies not generally taught in Western medical schools (according to current data available) and not generally prescribed by providers of medical care in Western tradition (i.e. medical care in the US). The use of CAM therapies is common amongst the general population (accounting for substantial expenditures) [10] and could be substantially more prevalent among people living with HIV/AIDS. [28,29,30,55] Limited evidence is available in the UK regarding the safe and effective use of CAM in the treatment of HIV/AIDS. Our results indicated that 85% of the participants did not believe CAM therapies cure HIV/AIDS. One can speculate that CAM therapies are used by HIV infected patients in this sample group not as an *alternative* to conventional treatment but to *complement* conventional treatment.

The use of CAM therapies by PLWHA and the known contraindications of certain ARV drug and some herbal remedies highlight the need to discuss CAM therapy use routinely as part of any discussion or treatment for HIV/AIDS patients. This might require physicians and other health care professionals to increase their knowledge about CAM therapies. However, there are still many gaps in our understanding of CAM therapies and possible interactions between ARV treatment and CAM therapies.

Based on the lack of evidence and following on from this study, one outcome of this project was the development of an algorithm (Appendix 6a and Appendix 6b) of CAM therapy use. This algorithm could be used to assess CAM therapy use amongst HIV positive patients. Physicians and other health care professionals would be able to determine the patterns and extent of CAM therapy use by the patients. Our findings, especially those regarding the contraindications of taking St. John's Wort in

conjunction with Nevirapine [35] and Indinavir [34], as well as garlic with Saquinavir [40] highlight the need for doctors and health care professionals to be aware of any CAM therapies that HIV positive patients are taking. Therefore the need for a CAM therapy algorithm. The algorithm illustrates the most well documented herbal remedies, drug-herb interactions as well as micronutrients and toxicity levels. The individual pathways for each CAM therapy are also shown and provide a quick reference tool to determine different outcomes are shown in the tool to assist health care providers to make decisions based on current evidence. In addition this algorithm may empower primary health care providers to manage a patient's treatment regimen with or without CAM therapy. A further audit process will be conducted to evaluate the effectiveness of the algorithm, its use among health care professionals and updating the algorithm as new data become available.

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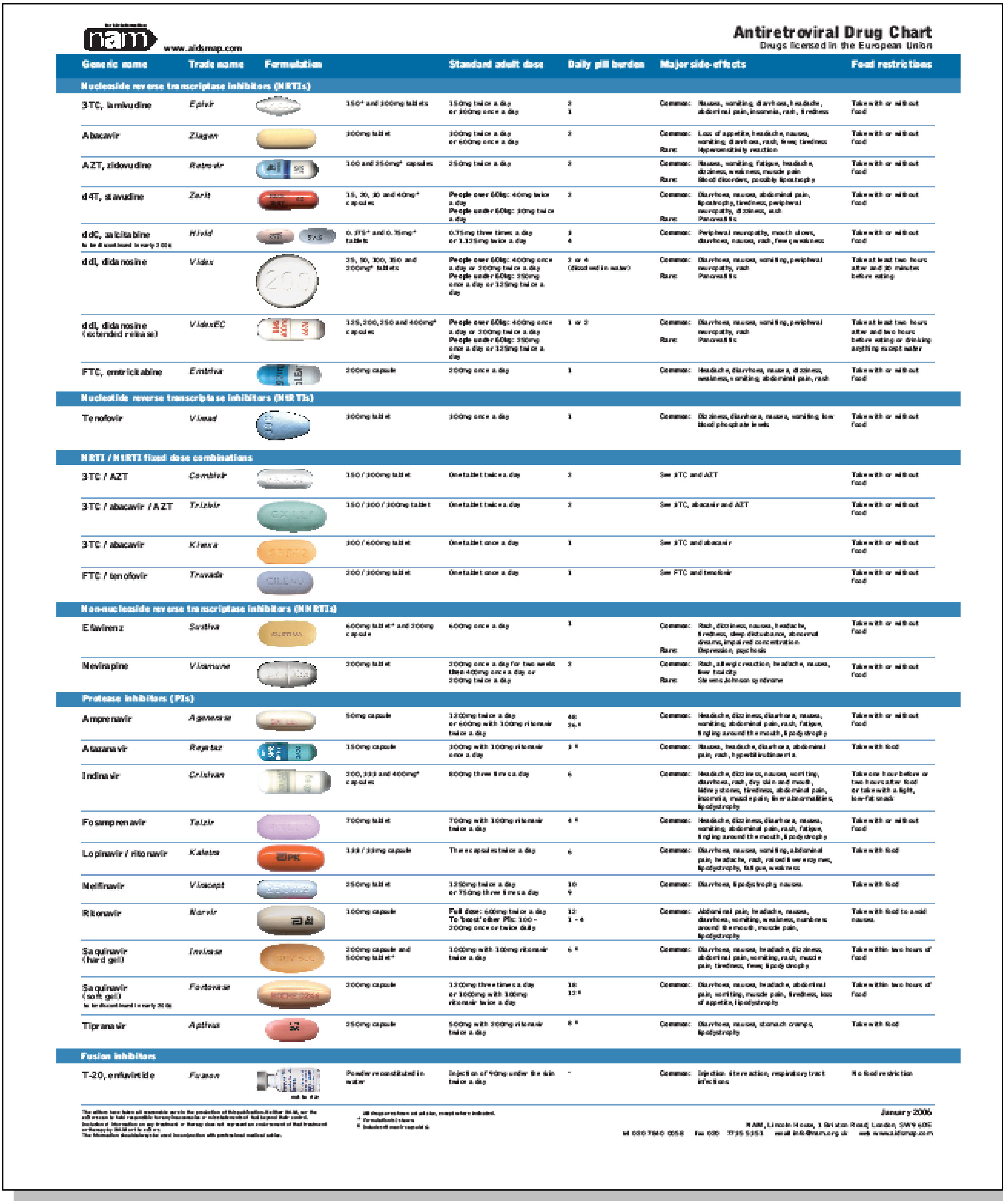
Appendix 1: Map of the London Boroughs

Appendix 2: Antiretroviral drug chart [4]



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Antiretroviral Drug Chart
Drugs licensed in the European Union

Generic name	Trade name	Formulation		Standard adult dose	Daily pill burden	Major side-effects	Food restrictions
Nucleoside reverse transcriptase inhibitors (NRTIs)							
3TC, lamivudine	*Epivir*		150* and 300mg tablets	150mg twice a day or 300mg once a day	2 1	Common: Nausea, vomiting, diarrhoea, headache, abdominal pain, insomnia, rash, tiredness	Take with or without food
Abacavir	*Ziagen*		300mg tablet	300mg twice a day or 600mg once a day	2	Common: Loss of appetite, headache, nausea, vomiting, diarrhoea, rash, fever, tiredness Rare: Hypersensitivity reaction	Take with or without food
AZT, zidovudine	*Retrovir*		100 and 250mg* capsules	250mg twice a day	2	Common: Nausea, vomiting, fatigue, headache, dizziness, weakness, muscle pain Rare: Blood disorders, possibly lipoatrophy	Take with or without food
d4T, stavudine	*Zerit*		15, 20, 30 and 40mg* capsules	People over 60kg: 40mg twice a day People under 60kg: 30mg twice a day	2	Common: Diarrhoea, nausea, abdominal pain, lipoatrophy, tiredness, peripheral neuropathy, dizziness, rash Rare: Pancreatitis	Take with or without food
ddC, zalcitabine to be discontinued in early 2006	*Hivid*		0.375* and 0.75mg* tablets	0.75mg three times a day or 1.125mg twice a day	3 4	Common: Peripheral neuropathy, mouth ulcers, diarrhoea, nausea, rash, fever, weakness	Take with or without food
ddI, didanosine	*Videx*		25, 50, 100, 150 and 200mg* tablets	People over 60kg: 400mg once a day or 200mg twice a day People under 60kg: 250mg once a day or 125mg twice a day	2 or 4 (dissolved in water)	Common: Diarrhoea, nausea, vomiting, peripheral neuropathy, rash Rare: Pancreatitis	Take at least two hours after and 30 minutes before eating
ddI, didanosine (extended release)	*VidexEC*		125, 200, 250 and 400mg* capsules	People over 60kg: 400mg once a day or 200mg twice a day People under 60kg: 250mg once a day or 125mg twice a day	1 or 2	Common: Diarrhoea, nausea, vomiting, peripheral neuropathy, rash Rare: Pancreatitis	Take at least two hours after and two hours before eating or drinking anything except water
FTC, emtricitabine	*Emtriva*		200mg capsule	200mg once a day	1	Common: Headache, diarrhoea, nausea, dizziness, weakness, vomiting, abdominal pain, rash	Take with or without food
Nucleotide reverse transcriptase inhibitors (NtRTIs)							
Tenofovir	*Viread*		300mg tablet	300mg once a day	1	Common: Dizziness, diarrhoea, nausea, vomiting, low blood phosphate levels	Take with or without food
NRTI / NtRTI fixed dose combinations							
3TC / AZT	*Combivir*		150 / 300mg tablet	One tablet twice a day	2	See 3TC and AZT	Take with or without food
3TC / abacavir / AZT	*Trizivir*		150 / 300 / 300mg tablet	One tablet twice a day	2	See 3TC, abacavir and AZT	Take with or without food
3TC / abacavir	*Kivexa*		300 / 600mg tablet	One tablet once a day	1	See 3TC and abacavir	Take with or without food
FTC / tenofovir	*Truvada*		200 / 300mg tablet	One tablet once a day	1	See FTC and tenofovir	Take with or without food
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)							
Efavirenz	*Sustiva*		600mg tablet* and 200mg capsule	600mg once a day	1	Common: Rash, dizziness, nausea, headache, tiredness, sleep disturbance, abnormal dreams, impaired concentration Rare: Depression, psychosis	Take with or without food
Nevirapine	*Viramune*		200mg tablet	200mg once a day for two weeks then 400mg once a day or 200mg twice a day	2	Common: Rash, allergic reaction, headache, nausea, liver toxicity Rare: Stevens Johnson syndrome	Take with or without food
Protease inhibitors (PIs)							
Amprenavir	*Agenerase*		50mg capsule	1200mg twice a day or 600mg with 100mg ritonavir twice a day	48 26 ¥	Common: Headache, dizziness, diarrhoea, nausea, vomiting, abdominal pain, rash, fatigue, tingling around the mouth, lipodystrophy	Take with or without food
Atazanavir	*Reyataz*		150mg capsule	300mg with 100mg ritonavir once a day	3 ¥	Common: Nausea, headache, diarrhoea, abdominal pain, rash, hyperbilirubinaemia	Take with food
Indinavir	*Crixivan*		200, 333 and 400mg* capsules	800mg three times a day	6	Common: Headache, dizziness, nausea, vomiting, diarrhoea, rash, dry skin and mouth, kidney stones, tiredness, abdominal pain, insomnia, muscle pain, liver abnormalities, lipodystrophy	Take one hour before or two hours after food or take with a light, low-fat snack
Fosamprenavir	*Telzir*		700mg tablet	700mg with 100mg ritonavir twice a day	4 ¥	Common: Headache, dizziness, diarrhoea, nausea, vomiting, abdominal pain, rash, fatigue, tingling around the mouth, lipodystrophy	Take with or without food
Lopinavir / ritonavir	*Kaletra*		133 / 33mg capsule	Three capsules twice a day	6	Common: Diarrhoea, nausea, vomiting, abdominal pain, headache, rash, raised liver enzymes, lipodystrophy, fatigue, weakness	Take with food
Nelfinavir	*Viracept*		250mg tablet	1250mg twice a day or 750mg three times a day	10 9	Common: Diarrhoea, lipodystrophy, nausea	Take with food
Ritonavir	*Norvir*		100mg capsule	Full dose: 600mg twice a day To 'boost' other PIs: 100 - 200mg once or twice daily	12 1 - 4	Common: Abdominal pain, headache, nausea, diarrhoea, vomiting, weakness, numbness around the mouth, muscle pain, lipodystrophy	Take with food to avoid nausea
Saquinavir (hard gel)	*Invirase*		200mg capsule and 500mg tablet*	1000mg with 100mg ritonavir twice a day	6 ¥	Common: Diarrhoea, nausea, headache, dizziness, abdominal pain, vomiting, rash, muscle pain, tiredness, fever, lipodystrophy	Take within two hours of food
Saquinavir (soft gel) to be discontinued in early 2006	*Fortovase*		200mg capsule	1200mg three times a day or 1000mg with 100mg ritonavir twice a day	18 12 ¥	Common: Diarrhoea, nausea, headache, abdominal pain, vomiting, muscle pain, tiredness, loss of appetite, lipodystrophy	Take within two hours of food
Tipranavir	*Aptivus*		250mg capsule	500mg with 200mg ritonavir twice a day	8 ¥	Common: Diarrhoea, nausea, stomach cramps, lipodystrophy	Take with food
Fusion inhibitors							
T-20, enfuvirtide	*Fuzeon*	not to size	Powder reconstituted in water	Injection of 90mg under the skin twice a day	-	Common: Injection site reaction, respiratory tract infections	No food restriction

The editors have taken all reasonable care in the production of this publication. Neither NAM, nor the editors can be held responsible for any inaccuracies or misstatements of fact beyond their control. Inclusion of information on any treatment or therapy does not represent an endorsement of that treatment or therapy by NAM or its editors. The information should only be used in conjunction with professional medical advice.

All drugs are shown at actual size, except where indicated.
* Formulation(s) shown
¥ Includes ritonavir capsule(s)

January 2006

NAM, Lincoln House, 1 Brixton Road, London, SW9 6DE
tel 020 7840 0050 fax 020 7735 5351 email info@nam.org.uk web www.aidsmap.com

Appendix 3: Information sheet

Whipps Cross University Hospital
Azalea Ward
Whipps Cross Road
Leytonstone
London E11 1NR

Tel: 020 8535 6705
Fax: 020 8535 6760

Project title:

A survey investigating the use of complementary and alternative therapies (CAM) among adult HIV-infected patients in an outpatient setting

You are being invited to take part in a study. Before you decide it is important for you to understand why the project is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this

What is the purpose of the project?

The term complementary and alternative therapies (CAM) are used to describe therapies other than conventional medical interventions (Anti – HIV treatment etc). Recent research has shown that the use of CAM among HIV infected people is on the increase. The high prevalence of CAM use among HIV infected patients suggests that complementary and alternative therapy use is an important part of their health management**.** The purpose of this research is to examine the use of complementary and alternative therapies among adult HIV-infected patients in an ethnically diverse population and to create an awareness of the potential drug-herb interactions among those patients using CAM therapies.

This study is conducted at the Department of Sexual Health in Whipps Cross University Hospital. All patients attending the clinic between August and November 2005 will kindly be asked to participate.

Why have I been chosen?

As a patient of DOSH (Department of Sexual Health) at Whipps Cross University Hospital you are invited to participate in this research to help us understand the role of complementary and alternative therapies in HIV/AIDS.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?

The study will be conducted as a questionnaire, and it will take you less than 20 minutes to complete the questionnaire. It will take 6 months to collect and analyse the data collected. Please be assured that your responses will be completely confidential.

What are the possible benefits of taking part?

There will be no direct benefits arising from your participation; however it might encourage sharing your complementary and alternative therapy (CAM) use with your clinic doctor/other health professional.

What if something goes wrong?

For negligent harm normal NHS indemnity applies as Whipps Cross University Hospital Trust sponsors this study.

There are no special arrangements to cover non-negligent harm. If a participant was harmed as a result of this study they may pursue a claim for negligence through litigation.

Will my taking part in this project be kept confidential?

All information that is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the hospital will have your name and address removed so that you cannot be recognised from it. Anonymised data will be stored on a personal computer, which is password protected. Completed questionnaires and consent forms will be kept in a locked filling cabinet at the Department of Sexual Health (DOSH). Anonymised data will be sent to the Department of Human Nutrition, University of Stellenbosch, South Africa for analysis.

Who is organizing and funding the project?

Department of Human Nutrition, University of Stellenbosch, South Africa.

What will happen to the results of the project?

Data will be reported in a thesis for the Master's degree in nutrition and submitted for publication in a peer-reviewed professional journal.

Who has reviewed the project?

The study was submitted for ethical approval at the NHS Central Office for Research Ethics Committee, as well as at the Committee for Human Research, Faculty of Health Sciences, University of Stellenbosch, South Africa.

Contact for Further Information

You can contact the principle investigator, Charlé Aucamp (Senior Dietitian) at 0208 535 6776 during office hours Monday to Friday, or by email at the following address: charle.aucampc@whippsx.nhs.uk if you have any further queries.

Thank you for your participation!

Appendix 4: Questionnaire

A survey investigating the use of complementary and alternative therapies (CAM) among adult HIV-infected patients in an outpatients setting

REFERENCE NUMBER: _____

PATIENT QUESTIONNAIRE

Have you ever used or are using complementary and alternative therapies (CAM)?

YES	NO

If **NO**, you do not need to complete this questionnaire. Thank you for your time.

If **YES**, please continue to **Section A.**

SECTION A: SOCIO-DEMOGRAPHIC INFORMATION

1. Which of the following best describes your education (*please tick*).

A. Secondary/ High School	1
B. College	2
C. University	3
D. Post Grad Education	4

2. Employment Status (*please tick)*

A. Full time paid employment	1
B. Part time paid employment	2
C. Self employed/freelance	3
D. Unemployed	4
E. Student	5

Please continue to section B (Page 3)

SECTION B: YOU AND HIV

3. How long have you been aware of your HIV status? (*please tick*)

A.	<3 months	1
B.	3 – 11 months	2
C.	1 – 5 years	3
D.	> 5 years	4

4. Your current state of health (*please tick*)

A.	Very poor	1
B.	Poor	2
C.	Fair	3
D.	Good	4
E.	Excellent	5

5. Are you currently using HIV medication?

YES	NO

If **NO**, please continue to **Section C**  **(PAGE 4)**

If **YES**, please continue to **Section D**  **(PAGE 7)**

SECTION C: I AM NOT CURRENTLY ON ANTI-HIV TREATMENT

6. Which of the following **complementary and alternative therapies** have you used in the past 6 months (*please tick all appropriate boxes)*

Alternative therapy	**Never used**	**Used in the past**	**Used at present**
Herbal Remedies			
Ayurvedic medicine			
Chinese medicine			
Tibetan medicine			
St. John's Wort			
Echinacea			
Ginseng			
Garlic			
Sutherlandia			
African Potato (Hypoxis)			
Other (*please specify*)			
Nutritional Supplements/Vitamins			
Selenium			
Glutamine			
Vitamins E			
Multivitamin/mineral supplement			
Other (*please specify*)			
Lifestyle/Homeopathy			
Prayer/ faith healing			
Meditation/ visualization			
Yoga			
Exercise			
Reiki			
Acupuncture			
Massage			
Chiropractic therapies			
Other (*please specify)*			

7. When did you start using these complementary and/or alternative therapies? (*please tick*)

   a. Before my HIV diagnosis 1

   b. After my HIV diagnosis 2

8. Why do you use complementary and/or alternative therapies? (*please tick all that apply*)

A. Dissatisfaction with conventional medication 1

B. You think it improves your general health and ensure long term survival 2

C. Family tradition/ Culture 3

D. Reduce the side effects of conventional medication 4

E. More personal control over your health care 5

F. You think it is more natural 6

G. Curiosity 7

H. I think it has anti- HIV properties 8

I. Other (*please describe*)
_____
_____
_____

9. Where do you get your information on alternative therapies? (*please tick all that apply*)

A. My Doctor/ nurse/ other health care professional 1

B. Alternative therapist 2

C. HIV positive friend 3

D. HIV/AIDS organization 4

E. Other friend/ relative 5

F. Traditional healer 6

G. Health Food Stores 7

H. Internet/articles/newspapers 8

I. Other, (*please specify*)
_____
_____
_____

10. On average, how much do you spend per month on complementary and/or alternative therapies? (*please tick*)

< £10	£11 – 20	£21 – 30	£31 – 40	£41 – 50	> £51

11. Did you consult your Doctor/other Health Care Professional before starting complementary and/or alternative therapies (*please tick)*

YES	NO

12. Are you aware of any possible drug interactions with complementary and/or alternative therapies especially herbal remedies? (*please tick*)

YES	NO

13. Do you belief complementary therapies and nutritional supplements cures HIV/AIDS?

YES	NO

THANK YOU FOR YOU PARTICIPATION

SECTION D: I AM CURRENTLY ON ANTI-HIV TREATMENT

14. For how long have you been on combination therapy? (*please tick*)

< 3 months	3-11 months	1-5 years	> 5 years

15. Which of the following symptoms did you experience in the past 6 months? (*please tick all that apply*)

10. Nausea	1
11. Vomiting	2
12. Loss of appetite	3
13. Diarrhoea	4
14. Constipation	5
15. Pain body/ muscle limb pain	6
16. Loss of taste/ smell	7
17. Other (*please specify*) _____	8

16. Which of the following **complementary and alternative therapies** have you used in the past 6 months (*please tick all appropriate boxes)*

Alternative therapy	**Never used**	**Used in the past**	**Used at present**
Herbal Remedies			
Ayurvedic medicine			
Chinese medicine			
Tibetan medicine			
St. John's Wort			
Echinacea			
Ginseng			
Garlic			
Sutherlandia			
African Potato (Hypoxis)			
Other (*please specify*)			
Nutritional Supplements/Vitamins			
Selenium			
Glutamine			
Vitamins E			
Multivitamin/mineral supplement			
Other (*please specify*)			

Lifestyle/Homeopathy			
Prayer/ faith healing			
Meditation/ visualization			
Yoga			
Exercise			
Reiki			
Acupuncture			
Massage			
Chiropractic therapies			
Other (*please specify)*			

17. When did you start using these complementary and/or alternative therapies? (*please tick*)

A. Before my HIV diagnosis 1

B. After my HIV diagnosis 2

18.Why do you use complementary and/or alternative therapies? (*please tick all that apply*)

A Dissatisfaction with conventional medication 1

B You think it improves your general health and ensures long term survival 2

C. Family tradition/ Culture 3

D. Reduce the side effects of conventional medication 4

E. More personal control over your health care 5

F. You think it is more natural 6

G. Curiosity 7

H. I think it has anti-HIV properties 8

I. Other (*please describe*)
_____
_____
_____
_____

19. Where did you get your information on complementary and alternative therapies? (*please tick all that apply*).

A. My Doctor/ nurse/ other health care professional 1

B. Alternative therapist 2

C. HIV positive friend 3

D. HIV/AIDS organization 4

E. Other friend/ relative 5

F. Traditional healer 6

G. Health Food Stores 7

H. Internet/articles/newspapers 8

I. Other, (*please specify*) 9

_____
_____
_____

20. On average, how much do you spend per month on complementary and/or alternative therapies? (*please circle*)

< £10	£11 – 20	£21 – 30	£31 – 40	£41 – 50	> £51

21. Did you consult your Doctor/other Health Care Professional before starting complementary and/or alternative therapies (*please tick)*

YES	NO

22. Are you aware of any possible drug interactions with complementary and/or alternative therapies especially herbal remedies? (*please tick*)

YES	NO

23. Do you belief complementary therapies and nutritional supplements cures HIV/AIDS?

YES	NO

THANK YOU FOR YOU PARTICIPATION

Appendix 5: Investigator data collection sheet

A survey investigating the use of complementary and alternative therapies (CAM) among adult HIV-infected patients in an outpatient setting

INVESTIGATOR DATA COLLECTION FORM

REFERENCE NUMBER: _____

DEMOGRAPHIC INFORMATION

1. Gender (*please tick*)

MALE	FEMALE

2. Age: _____

3. Which ethnic group does the patient belong to? (*please tick*)

White	British	1
	Irish	2
	Other White, please specify_____	3
Mixed	White and Black Caribbean	4
	White and Black African	5
	White and Asian	6
	Other mixed, please specify_____	7
Asian/British Asian	Indian	8
	Pakistani	10
	Bangladeshi	11
	Other Asian, please specify_____	12
Black or Black British	Caribbean	13
	African	14
	Other Black, please specify_____	15
Other ethnic categories	Chinese	17
	Any other, please specify_____	
Not stated	Not stated	

4. Is the participant currently using HIV combination therapy? (*please tick*)

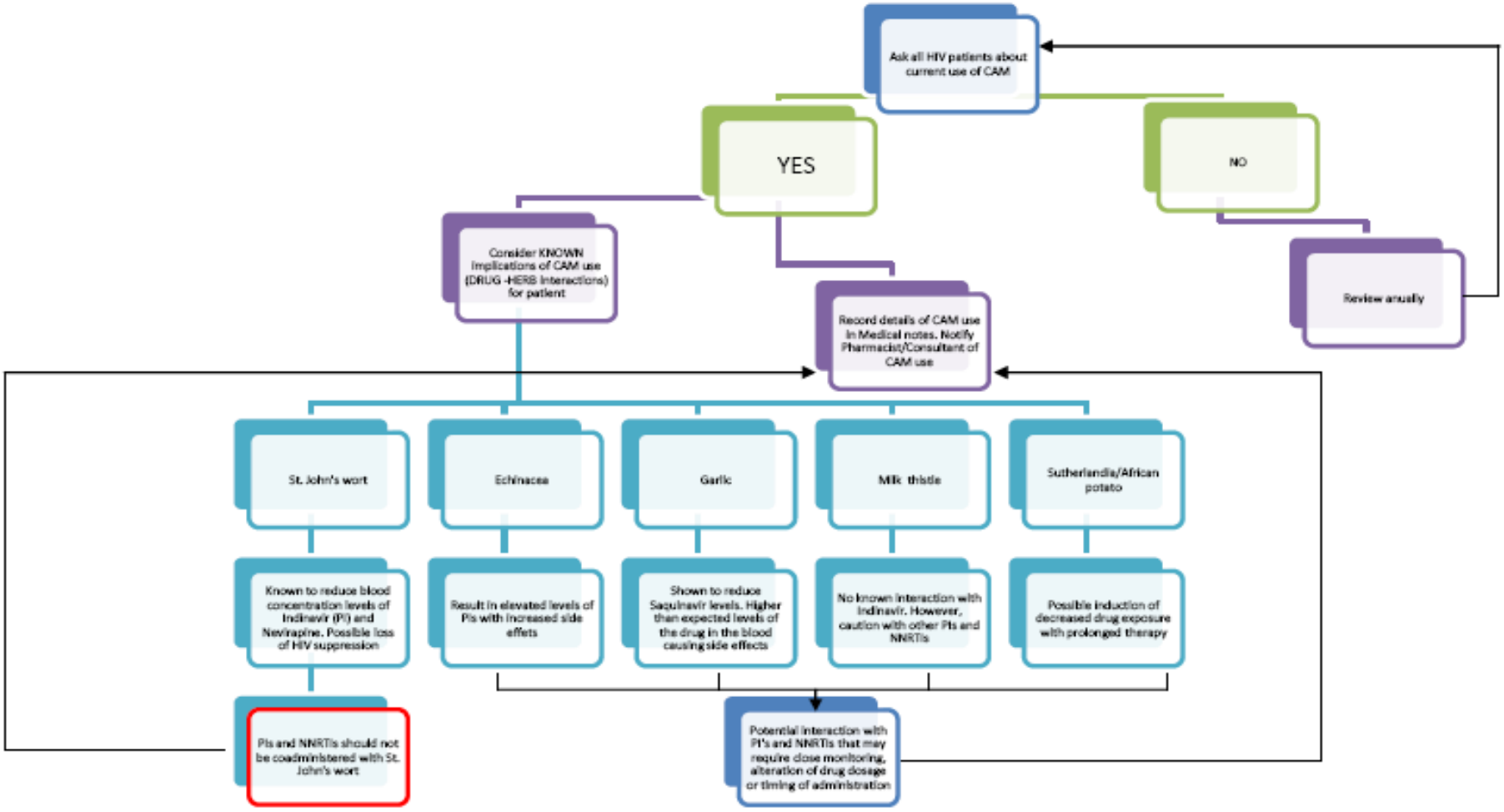
YES	NO

If **NO,** you have collected all the data

If **YES**, which combination: (*please circle*)

NRTI's	NNRTI's	PI's	Dual and boosted Protease combinations	Entry Inhibitors (fusion inhibitors)
D4T (Zerit, stavudine)	Efavirenz (sustiva)	Indinavir (crixivan)	Lopinavir/r (kaletra)	Enfuvirtide (T-20, fuzeon)
AZT (Retrovir, zidovudine	Nevirapine (viramune)	Nelfinavir (viracept)	Indinavir/ritonavir	
ddI (videx, didanosine)	Delavirdine (rescriptor)	Atazanavir (reyataz)	Saquinavir/ritonavir	
3TC (epivir, lamivudine)			Fosaprenavir/ritonavir	
Abacavir (Ziagen)			Atazanavir/ritonavir	
Combivir (AZT/3TC)			Tipranavir/ritonavir	
Trizivir (AZT/3TC/abacavir)				
Tenofovir (viread)				
FTC (emtracitabine)				

Appendix 6a: Algorithm for CAM therapy use in DOSH (Herbal remedies)



Appendix 6b: Algorithm for CAM therapy use in DOSH (Micronutrients)