NUTRITION COUNSELING IN ADULTS INFECTED WITH THE HUMAN IMMUNODEFICIENCY VIRUS

A SYSTEMATIC REVIEW OF RANDOMISED CONTROLLED TRIALS

A dissertation prepared by JOYCE KOECH CHIRJOY003 in partial fulfillment of the requirements for the Master of Public Health (MPH) from The University of Cape Town

March 2006
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DECLARATION

I, Joyce Koech hereby declare that this dissertation is my original work (except where acknowledgements indicate otherwise) and that neither the whole nor any part of it has been, is being or is to be submitted for another degree in this or any other university.

________________________
Signature

________________________
Date
ACKNOWLEDGEMENTS

I am grateful to Professor Jimmy Volmink (JV) Faculty of Health Sciences, Stellenbosch University, SA for his expert advice and guidance in the development of the protocol and data extraction for this review, Nancy Santesso for her help in developing the search strategy, Mark Engel, Primary Healthcare Directorate, University of Cape Town, SA for his assistance in data analysis, my supervisor James Irlam (JI), Primary Healthcare Directorate, University of Cape Town, SA for his continued guidance and support throughout the review process and my husband and sons for their unwavering encouragement and support.
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ABSTRACT

Background
HIV-infected individuals may be at nutritional risk at any point in the course of their illness. Nutrition counseling has been found to be an important intervention for maintaining and improving nutritional status in HIV infection. The evidence for the magnitude of benefit has not previously been systematically reviewed.

Objectives
To assess the effectiveness of nutritional counseling in improving dietary intake and nutritional status in HIV-infected adults

Methods
Eligible studies were identified from comprehensive searches of electronic databases and conference proceedings for all randomised controlled trials (RCTs) of nutrition counseling compared with either no nutrition counseling, oral supplements, or with nutrition counseling plus oral supplements. Two reviewers independently assessed the eligibility of the studies and their methodological quality, and extracted data on participants, interventions and outcomes. A meta-analysis of data on nutritional status and dietary intake was performed.

Results
Three studies with a total of 238 participants were included in the review. All three studies compared nutrition counseling with nutrition counseling plus oral supplements. Data were available from all three studies for changes from baseline in weight, lean body mass and body fat. In one study the changes in both groups were significant, but the differences between groups did not reach statistical significance. Energy intake data were available from 2 studies, and both showed a significant increase from baseline in both groups. The inter-group difference was significantly higher overall in the group receiving
counseling and supplements (weighted mean difference (WMD) 4.40 kcal/kg (95% CI 1.09 to 7.70 in meta-analysis). Protein intake data were available from one study and showed higher protein ingestion in the counseling plus supplement group of 22g/day (95% CI 6.01 to 37.99). No data were available for mortality, and limited outcomes data on morbidity, CD4 cell counts, viral load, grip strength, cognitive function, and quality of life showed no differences in either group from baseline.

Discussion

The results of this review suggest that nutrition counseling, with or without supplements, improves baseline dietary intake and nutritional status, and that counseling in conjunction with supplements may be more beneficial than counseling alone in improving dietary intake. Nutrition counseling alone should however be maintained in the absence of nutrition supplements, as it has been shown to hold additional benefits such as increased awareness of nutritional needs, promotion of positive nutritional practices, and emotional support for HIV-infected individuals. Adequately powered trials with sufficient duration of follow-up are required that compare the effect of nutrition counseling versus different forms of nutrition therapy on clinical outcomes in HIV infection.
BACKGROUND

Adequate nutrition plays a fundamental role in prolonging survival and improving the quality of life of people infected with Human Immunodeficiency Virus (HIV) (Elbein, 1995). In HIV-infected individuals there is a cyclical relationship between the HIV infection and nutritional status. Decreased intake of food, heightened use of nutrients in the body, an increase in resting energy expenditure, metabolic changes, and rapid loss of nutrients from the body as a result of HIV infection, all lead to a weakened immune system and therefore contribute to recurring infections and further disease progression (Department of Health, 2001; Piwoz, 2004).

Metabolic changes occur in HIV infection, as in other infections, due to the release of cytokines, which are known to alter metabolic states by promoting anorexia, increasing protein catabolism and increasing hypertriglyceridemia (Stack, 1996). The consequence of these factors is malnutrition, which can contribute to compromised host immune function, damage to organs, poor response to treatment, and progressive debilitation (Salomon, 2002). Malnutrition in HIV infection is mainly characterized by wasting, a common syndrome that occurs as a result of decreased food consumption caused by loss of appetite, mouth and throat sores, and side-effects of medication, among other factors (Piwoz, 2004; Romeyn, 1998). Wasting has been defined by the Centre for Disease Control and prevention (CDC) as more than 10% involuntary loss in body weight (McKinley, 1994). Body weight is the total body mass comprising lean body mass and body fat (Kotler, 1997).

There appears to be an increased risk of opportunistic infections and shorter survival time in HIV-infected individuals with weight loss and wasting, irrespective of immune status, than in those with normal nutritional status (Nerad, 2003). In HIV infection,
immune status is influenced by a number of defects in the body’s natural defense mechanism. There is not only a deficiency in the number of cells to fight infection, but the ones that are present are not fully functional. (Walker, 2000). Additionally, HIV-infected individuals with compromised micronutrient status have been shown to have poorer clinical outcomes than those with better micronutrient status (Piwoz, 2004).

Survival time is cut short due to death from wasting, which occurs as a result of a disproportionate depletion of body cell mass to loss of lean body mass and body fat (McKinley, 1994). It has been shown that death in HIV-infected individuals occurs when loss of lean body mass equals 54% of normal (Stack, 1996).

As HIV-infected individuals may be at nutritional risk at any point in the course of their illness, it is recommended that nutritional support be commenced as early as possible (Bijlsma, 2000; Nerad, 2003), and nutritional status monitored closely from the time of diagnosis (van Niekerk, 2000). Nutritional support includes nutrition supplements for specific micronutrient deficiencies, food-based interventions in food-insecure situations, and nutrition counseling on specific behaviors (Piwoz, 2004).

HIV-infected individuals often have concurrent multiple micronutrient deficiencies (Bijlsma, 2000). Evidence from some observational (Stack, 1996; van Niekerk, 2000) and experimental studies (Piwoz, 2004; Schwenk, 1999) suggests that supplementation with micronutrients may slow the progression of HIV disease and therefore provide an effective, low-cost means of delaying the initiation of antiretroviral therapy. A systematic review of 18 trials of micronutrient supplementation in children and adults with HIV infection found insufficient evidence that micronutrient supplementation is clinically beneficial in adults however, but did find clear evidence for vitamin A supplementation in children. The review endorses the WHO recommendation that everything possible
should be done to support adequate dietary intake of micronutrients at recommended daily allowance (RDA) levels (Irland, 2005).

HIV/AIDS greatly impacts on household food security, as infected individuals and family members are sometimes unable to work for extended periods of time, undermining earnings and food production activities in the home (FANTA, 2000). Food-based interventions, such as food aid, may help to mitigate this situation by ensuring that food is available, accessible and properly utilized by infected individuals and their families. Giving food and psycho-social support may therefore help to improve nutrition and delay progression of HIV disease (FANTA, 2000).

In addition to nutrition supplements and food-based interventions, nutrition counseling is proposed as an important intervention in HIV infection (Piwoz, 2004). Nutrition counseling is a set of communication activities that seek to bring about a voluntary change in nutrition-related behavior in order to improve nutritional status and quality of life. Counseling includes information and culturally appropriate advice on preparing nutritionally adequate and affordable meals, making healthy food choices, practicing food safety to prevent food-borne infections, and optimizing and maintaining nutritional status in simple and practical ways (Bijlsma, 2000; FANTA, 2004; van Niekerk, 2000).

Nutrition counseling is considered useful through all the stages of HIV infection. In the asymptomatic stage, counseling that promotes positive living should be provided. This refers to counseling that emphasizes a normal and healthy eating pattern that encompasses a wide variety of healthy foods. In the symptomatic stage, advice about the nutritional management of HIV-related opportunistic infections, symptoms, and medications is appropriate. This includes counseling to manage nutrition-related
symptoms of common HIV-related illnesses and to help HIV-infected individuals and their households to optimally use available foods to manage symptoms and uphold food intake. At the stage of "full blown" AIDS, nutritional management of antiretroviral (ARV) therapy, where available, is appropriate. This is because in some cases the use of ARVs has been known to cause side effects such as nausea and vomiting, which may compromise dietary intake and consequently nutritional status if the situation is not effectively managed. Nutritional management that includes the provision of information and support by means of community-based care programs and food assistance is recommended to help HIV-infected individuals on ARV treatment to manage drug side effects and to prevent drug-food interactions (Department of Health, 2001; Piwoz, 2004).

The evidence for the benefits of nutrition counseling has been reviewed in relation to general illness-related malnutrition (Baldwin, 2001) and to HIV infection (Nerad, 2003). Baldwin (2001) concluded that there was a lack of evidence from a Cochrane systematic review of randomised controlled trials (RCTs) for the effect of dietary advice on survival and morbidity, but that dietary advice combined with oral nutritional supplements may be more effective than advice alone in enhancing short-term weight gain and energy intake in people with illness-related malnutrition.

Nerad (2003) reviewed RCTs and observational studies of nutritional interventions in HIV-infected adult patients and concluded that dietary counseling has been shown to improve health outcomes, especially when combined with oral nutritional supplements. The review included a study of patients' charts in a reproductive health clinic at the New York Hospital (McKinley, 1994). It showed that those who received an individualized care plan developed by a dietician plus educational materials on menu patterns and food
handling gained weight (a 1.3% increase from baseline), while those without counseling saw a 2% decrease, although the difference did not reach statistical significance (p<0.2).

Another study in a public hospital in Johannesburg, South Africa that compared nutrition counseling against no counseling without any supplements (Van Nierkerk, 2000) found that increase in body weight was significantly greater in counseled patients compared to those receiving no counseling (p<0.01); moreover patients who maintained or gained weight had a 45% decrease in the incidence of opportunistic infections and lower CD4 counts. Similarly, a follow-up study that was carried out at the Deaconess Hospital in Boston, U.S.A concluded that HIV-infected patients without secondary infections could gain or maintain weight through receiving nutrition counseling combined with the use of an oral nutritional supplement that was high in energy and protein. The results of the study show that over 70% of the patients who received the intervention were able to maintain or gain weight (Stack, 1996). Finally, a 12-week study conducted in a Swiss hospital found that nutritional intervention in HIV-infected individuals with oral nutritional supplements (2510 kJ complete macro- and micronutrients) combined with dietary counseling, decreased whole body protein catabolism, increased measurements of lean body mass, and decreased body fat mass (Berneis, 2000).

The review by Nerad was not a systematic review however, in that no description was given of the methods used to search for, select, and appraise the quality of the studies reviewed, which renders it susceptible to selection bias. The evidence from good-quality RCTs on the effectiveness of nutritional counseling in adults with HIV infection therefore awaits systematic review.
OBJECTIVES OF REVIEW

To assess the effectiveness of nutritional counseling in improving dietary intake and nutritional status in HIV-infected adults.

METHODS

Criteria for Considering Studies for this Review

Types of studies
Randomised controlled trials (RCTs) in adults with HIV infection, in any language.

Types of interventions
Nutrition counseling, defined as advice that seeks to improve the quantity and quality of dietary intake, compared with either no nutrition counseling; oral nutritional supplements only (defined as a dietary supplement of any duration for increasing the total daily intake in order to manage disease-related malnutrition); or nutrition counseling plus oral nutritional supplements.

Types of outcome measures
Primary outcomes assessed included mortality; morbidity (frequency; type and duration of episodes of opportunistic infections; AIDS-defining infections; other types of illness as measured in the studies; and frequency of hospital admissions); measures of nutritional status, such as change in body weight or body mass index (BMI); and dietary intake.

Secondary outcomes included markers of immune response (e.g. CD4 counts); levels of viral load; and any adverse effects of the interventions.
Search Strategy for Identification of Studies

All RCTs comparing the effects of nutrition counseling with no nutrition counseling, oral supplements, or with nutrition counseling in conjunction with oral supplements, were identified from searches of the electronic databases of the Cochrane Central Register of Controlled Trials (issue 4, 2005); CINAHL; OVID; and EMBASE. The searches were conducted in November 2005 using the search terms listed in Appendix 2.

In addition, the Internet was searched for proceedings of the International Conference on Nutrition and HIV Infection (1997-2003); the International AIDS Conference (1994 - 2004); and the International Conference on HIV/AIDS and Food and Nutrition Security, (2005). The reference lists of all studies included in the review were also scanned for further studies.

Data Extraction

One reviewer (JK) reviewed the titles and abstracts from each search for potentially eligible studies using the pre-defined eligibility criteria. The potentially eligible studies (n=11) were assessed by two reviewers (JV, JK) against the inclusion criteria. Two reviewers (JL, JK) independently appraised the methodological quality and extracted the data from the included studies, and any disagreements were resolved by discussion.

The assessment of the methodological quality of each study was based on the standard methods of the Cochrane Collaboration, namely the method of randomisation, concealment of the allocation sequence from those enrolling participants, blinding of the outcome assessors, and the percentage of participants lost to follow up.
Data on study participants, interventions, and outcomes of the three eligible studies were extracted using a pre-piloted data extraction form. Outcomes data, where available, were entered into the Review Manager software (RevMan Version 4.2 for Windows) for assessing clinical homogeneity between the studies and for producing the meta-analysis "forest plots" (Figures 1, 2). Continuous data were combined from the three studies to produce weighted mean differences (WMD). Precision of the estimates of effect was represented by means of 95% confidence intervals.
RESULTS

Three studies comprising of 238 randomised participants fulfilled the inclusion criteria for this review (De Luis, 2003; Schwenk, 1999; Rabeneck, 1998) (Table 1) and eight studies were excluded that did not meet the inclusion criteria for the reasons given in Appendix 1, 'Characteristics of excluded studies'. The methods of randomisation and allocation concealment were unclear in all studies as insufficient details were provided. One study (De Luis, 2003) reported that blinding of outcome assessors was not performed. Follow-up ranged from 6 weeks to 3 months and loss to follow up from 6% to 16%.

The participants in the studies were all HIV-infected adults, the majority of them men, at various stages of HIV infection, in settings that included several outpatient clinics and a number of private practices in Houston, U.S.A (Rabeneck, 1998), a German outpatient clinic (Schwenk, 1999), and a Spanish outpatient clinic (De Luis, 2003) In two studies (De Luis, 2003; Schwenk, 1999), all participants were on antiretroviral treatment.

All three studies compared nutrition counseling to increase dietary intake alone versus nutrition counseling plus oral supplements. The oral supplements used were a standard enteral formula (De Luis, 2003); a range of fortified drinks or semi-liquid dessert with a soy protein basis or a maltodextrin-based fruit drink (Schwenk, 1999); and a specialized medium-chain triglyceride formula suitable for HIV-infected patients with fat malabsorption (Rabeneck, 1998).

Data were available from the three studies for changes in nutritional status from baseline, namely weight, lean body mass and body fat. The changes from baseline were significant for both groups in all outcomes in one study (De Luis, 2003), but there were no
significant inter-group differences in any outcomes in any of the studies, as indicated by the meta-analysis (Figure 1): weight, WMD 0.29 kg (95% CI -0.51 to 1.09); lean body mass, WMD 0.59 kg (-0.69 to 1.87); and body fat, WMD -0.05 kg (95% CI -0.92 to 0.81).

Data were available for energy intake from two studies (De Luis, 2003; Schwenk, 1999). The changes from baseline were significant for both groups in both studies, with the counseling and supplements group benefiting significantly more overall than the counseling only group (meta-analysis WMD 4.40 kcal/kg (95% CI 1.09 to 7.70), figure 2).

Protein intake data were available from one study (De Luis, 2003), and showed a significant improvement in protein ingestion in the counseling and supplement group of 22g/day (95% CI 6.01 to 37.99), as compared to the counseling only group.

No deaths occurred in any of the studies. Schwenk et al (1999) reported four hospital admissions for opportunistic infections, three in the counseling group and one in the counseling plus oral supplements group. The other two studies did not report any clinical outcomes. Data on changes in CD4 cell counts and viral load were available from one study (De Luis, 2003), which showed that they remained stable throughout the three month study period, from 431 (254) to 457 (229) in group one and 621 (288) to 559 (330) in group two. Adverse effects of supplements, namely nausea, epigastric burning and dislike of taste, were reported by one study in one individual each (Rabeneck, 1998).

Rabeneck (1998) also reported on the effects on grip strength, quality of life and cognitive function. Patients in the supplemented group had a greater but non-significant increase in grip strength compared to controls (median changes from baseline were 2.8 kg versus 0.7 kg), and experienced non-significant improvements in short-term and long-term memory tests. There was no difference in total quality-of-life scores between the groups.
<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>Interventions</th>
<th>Primary Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Luis 2003</td>
<td>Adults (n=70), 56 men 14 women, mean age (SD)</td>
<td>Nutrition counseling and dietary guidelines to achieve normal caloric intake</td>
<td>Survival, changes in weight, protein intake, carbohydrate intake and CD4 cell counts, viral load were using standardised measurement procedures.</td>
<td>Caloric ingestion increased by 486 cal/day in counseling plus supplement group and 93 cal/day in counseling group. Protein ingestion increased by 23g/day and 1g/day respectively. Weight increase by 2.75% in counseling plus supplement group (p&lt;0.05) and a 10.8%, p&lt;0.05 increase in lean body mass. There was no statistically significant difference in group 2 in weight and lean body mass measures.</td>
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<td></td>
<td>dietary counseling group 39.9 years (9) and dietary counseling plus supplements group mean age 37.5 years (11) with HIV infection and had lost 5% or more of usual weight in past 6 months. With or without AIDS. All participants were on ARV treatment. A 24 hour dietary history was performed at baseline and at 3 months. The study was conducted in a Spanish outpatient clinic.</td>
<td>versus nutrition counseling plus oral supplements of specialized medium-chain triglyceride formula, fortnightly for six weeks.</td>
<td></td>
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</tr>
<tr>
<td>Rabeneck 1998</td>
<td>Adults (n=118), all men, mean age (SD) dietary counseling group 41.1 years (9.7) and dietary counseling and supplement group 39.3 years (8.8 years) with HIV infection who had involuntary weight loss of &gt; 10% in last 6 months and were &lt; 90% of usual weight for height. 12 dropouts in nutrition counseling group (20%) and 16 dropouts in nutrition counseling plus supplement group (27%). Initial assessment included a 24 hour diet history. The study was conducted in several outpatient clinics and a number of private practices in Houston, U.S.A.</td>
<td>Individualized nutrition counseling by a study dietitian to achieve a specific energy target versus nutrition counseling plus oral supplements of specialized medium-chain triglyceride formula, fortnightly for six weeks.</td>
<td>Body fat, change in weight, lean body mass, grip strength, skin fold measures, quality of life, cognitive function, using standardised measurement procedures.</td>
<td>The means and std deviations for outcomes in the supplement group and the control group respectively were weight, 63.3(9.4) and 65.7(9.2), BMI, 20.6(3.0) and 21(2.6), Grip strength, 40.9(8.6) and 41(10.7), Body fat, 22.8(4.9) and 23.4(4.1), lean body mass 48.7(5.9) and 50.1(6.3)</td>
</tr>
<tr>
<td>Schwenk</td>
<td>HIV positive adults (n=50, 47 men, 3 women, mean (SD) age for dietary counseling group 39.5 years (10.2 years) and 39.4 years (9.2 years) in supplement group who had lost &gt;5% of usual weight and were actively losing weight, &gt;3% in last month. 3 drop outs in counseling group and 2 in supplement group. All participants were on ARV treatment. Initial assessment included a 24 hour diet history. The study was conducted in a German outpatient clinic.</td>
<td>Individualised nutrition counseling by one dietician and a list of household measures to increase energy intake by 600 kcal/day using normal food versus nutrition counseling plus oral nutrition supplements (0.6-1.5 kcal/ml) fortnightly for 8 weeks</td>
<td>Survival, change in body cell mass, change in weight, change in energy intake, hospital admissions, and incidence of AIDS, using standardised measures.</td>
<td>-Lean body mass increased from baseline in both groups, p&lt;0.05 with no difference between groups -Total energy intake higher in supplement group, p&lt;0.01 and kilo calorie intake higher in supplement group by 11(6) kcal/kg</td>
</tr>
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</table>
DISCUSSION

This review aimed to determine the effectiveness of nutrition counseling in improving nutrition intake and nutritional status in adults infected with HIV by means of a systematic review of RCTs of adequate methodological quality.

The three trials included in this review had a number of methodological limitations, in that they were all of short duration, had small sample sizes, and varied with respect to the intensity of counseling and composition of nutrition supplements. Additionally, one study (Rabeneck, 1998) had a high loss to follow up rate (27%) in the nutrition counseling group. The methods used in trials to minimize bias, such as concealment of the random allocation schedules, and blinding, were not clearly reported in all studies, or were not performed, which may compromise the validity of the outcomes.

Despite these limitations, this review provides some evidence of the benefits of nutrition counseling, with or without supplements, on nutritional status (body weight, lean body mass, and body fat) and dietary intake (energy and protein intake), with only minor adverse effects of supplementation. It also indicates that nutrition counseling may be more beneficial in conjunction with oral supplements than nutrition counseling alone. No evidence of effect on any other outcomes (mortality, morbidity, CD4 counts, or viral load, cognitive function, grip strength, or quality of life) was found, although the trials were insufficiently powered to detect small effects.

These findings are consistent with a number of observational studies (McKinley, 1994; Stack, 1996; van Niekerk, 2000; Berneis, 2000) and reviews of studies in people with HIV.
Implications for Practice

Nutrition counseling is recommended to improve nutrition intake and nutritional status in HIV-infected people, even in the absence of nutritional supplements, as it has been shown to also increase awareness of nutritional needs, promote positive nutritional practices, and provide emotional support for HIV-infected individuals (Schwenk, 1999; van Niekerk, 2000; McKinley, 1994). Nutrition counseling should be started as early as possible in the course of illness and be directed at the cause of malnutrition. Furthermore, good nutrition counseling should be affordable, practical and culturally relevant (van Niekerk, 2000).

In developing countries especially, it is important to incorporate nutrition counseling and support in the care of HIV-infected individuals in the health system in order to empower individuals to make informed and appropriate dietary choices (van Niekerk, 2000). In South Africa, as in many other developing countries, the Department of Health (DoH) has therefore developed guidelines on nutrition and HIV infection for people living with HIV/AIDS. These guidelines explain how to address the nutritional aspects of HIV-related conditions and provide practical recipes using locally available foods, as well as simple home remedies for easing some of the problems people with HIV/AIDS may experience (Department of Health, 2001). These guidelines need to be supported by programs to ensure proper implementation, such as the training of health workers and the development of comprehensive health promotion strategies (Bijlsma, 2000).
Anti-retroviral drugs (ARVs) are becoming more and more accessible to HIV-infected individuals. As a result of this, it has become apparent that the interactions between food and ARVs can have both positive and negative effects on individuals. In nutrition counseling it is critical to understand the specific nutritional interactions and their implications so as to help infected individuals maintain good nutritional status and to improve drug efficacy and tolerance (FANTA, 2003).

It is therefore appropriate to support the recommendations of the World Health Organization (WHO) that nutrition counseling and support, which incorporates dietary recommendations, food safety recommendations and recommendations for the treatment and management of infections, should be given to all HIV-infected individuals, whether on ARV treatment or not (WHO, 2005). Nutrition counseling and support are useful in all stages of HIV infection and should be provided in the clinic, community and in home-based care programs. It should be preceded by a nutritional assessment, which is a fundamental part of HIV care and should be carried out regularly at all levels of the health system. Where malnutrition and food shortages are likely to occur, for instance among vulnerable groups such as pregnant women, breastfeeding mothers, and young children, targeted food supplements should be provided and therapeutic feeding should continue for severely malnourished individuals, alongside treatment of HIV infection (WHO, 2005).

Implications for Research

The availability and affordability of quality nutrition counseling may be a problem in countries with limited resources, and research is therefore needed on ways to make these services more available and affordable. Furthermore, large, adequately-powered trials with sufficient duration of follow-up are required that compare the effects of nutrition
counseling with different forms of nutrition therapy on clinical outcomes in adults with HIV infection.
REFERENCES


<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
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<tr>
<td>Batterham 2001</td>
<td>Incorrect comparison (nutrition counseling versus appetite stimulants)</td>
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<tr>
<td>Berneis 2000</td>
<td>Comparison does not meet inclusion criteria</td>
</tr>
<tr>
<td>Chlebowski 1995</td>
<td>Not a randomised controlled trial</td>
</tr>
<tr>
<td>Karsegard 2004</td>
<td>Comparison does not meet inclusion criteria</td>
</tr>
<tr>
<td>Keithley 2002</td>
<td>Comparison does not meet inclusion criteria</td>
</tr>
<tr>
<td>McKinley 1995</td>
<td>Not a randomised controlled trial</td>
</tr>
<tr>
<td>Melchior 1996</td>
<td>Randomised controlled trial of total parenteral nutrition</td>
</tr>
<tr>
<td>Stack 1996</td>
<td>Not a randomised controlled trial</td>
</tr>
<tr>
<td>Van Nierkek 2000</td>
<td>Not a randomised controlled trial</td>
</tr>
</tbody>
</table>
A. OVID MEDLINE Search Terms

1. exp nutrition/
2. exp dietetics/
3. exp nutrition therapy/
4. exp dietary services/
5. eating/
6. exp food/
7. exp feeding behavior/
8. dh.fs.
9. ((nutrition$ or diet$ or food$) adj3 (therap$ or advice or counsel$ or service$)).tw.
10. ((nutrition$ or diet$ or food$) adj3 supplement$).tw.
11. or/1-11
12. limit 12 to aids
13. randomised controlled trial.pt.
14. controlled clinical trial.pt.
15. randomised controlled trials.sh.
16. random allocation.sh.
17. double blind method.sh.
18. single-blind method.sh.
19. or/1-6
20. (animals not human).sh.
21. 7 not 8
22. clinical trial.pt.
23. exp clinical trials/
25. ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
26. placebo$ .ti,ab.
27. placebos.sh.
28. random$.ti,ab.
29. research design.sh.
30. or/10-17
31. 18 not 8
32. 19 not 9
33. comparative study.sh.
34. exp evaluation studies/
35. follow up studies.sh.
36. prospective studies.sh.
37. (control$ or prospectiv$ or volunteer$).ti,ab.
38. or/21-25
39. 26 not 8
40. 27 not (9 or 20)
41. 9 or 20 or 28
B. CINAHL Search Terms
(cumulative Index to Nursing & Allied Health) 1982 to November Week 3 2005

1. exp nutrition/
2. exp nutrition services/
3. exp dietetics/
4. exp diet therapy/
5. exp nutrition education/
6. exp eating/
7. exp eating behavior/
8. exp food/
9. dh.fs.
10. ((nutrition$ or diet$ or food$) adj3 (therap$ or advice or counsel$ or service$)).tw.
11. ((nutrition$ or diet$ or food$) adj3 supplement$).tw.
12. or/1-11
13. exp hiv infections/
14. exp Acquired Immunodeficiency Syndrome/
15. exp Human Immunodeficiency Virus/
16. (hiv$ or aids).tw.
17. ((acquired or human) and immun$).tw.
18. or/13-17
19. 12 and 18
20. exp clinical trials/
22. random$.mp.
23. ((single or double) adj (blind$ or mask$)).mp.
24. placebo$.mp.
25. or/20-24
26. 19 and 25
C. Search terms for CENTRAL REGISTER OF CONTROLLED TRIALS

1. (hiv$ or aids).mp.
2. ((acquired or human) and immun$).mp.
3. (nutri$ or diet$ or food$ or supplement$ or intake$).mp.
4. dh.fs.
5. or/1-2
6. or/3-4
7. 5 and 6
D. EMBASE Search terms
1980 to 2005 Week 47

1. exp nutrition/
2. nutritional health/
3. DIETETICS/
4. dietitian/
5. ((nutrition$ or diet$ or food$) adj3 (therap$ or advice or counsel$ or service$)).tw.
6. ((nutrition$ or diet$ or food$) adj3 supplement$).tw.
7. or/1-6
8. exp Human Immunodeficiency Virus/
9. exp Human Immunodeficiency Virus Infection/
10. exp Acquired Immune Deficiency Syndrome/
11. (hiv$ or aids).tw.
12. ((acquired or human) and immun$).tw.
13. or/8-12
14. 7 and 13
15. exp clinical trial/
16. random$.mp.
17. placebo$.mp.
18. ((single or double) adj (blind$ or mask$)).mp.
19. or/15-18
20. 14 and 19
Figure 1: Changes from baseline in nutritional status

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Treatment Mean (SD)</th>
<th>Control Mean (SD)</th>
<th>WMD (fixed) 95% CI</th>
<th>Weight %</th>
<th>WMD (fixed) 95% CI</th>
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<tr>
<td>Review:</td>
<td>Nutrition Counselling To Improve Clinical Outcomes In People Infected With The Human Immunodeficiency Virus</td>
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<td>Comparison:</td>
<td>02 Nutritional counselling vs Nutritional counselling + Oral supplements</td>
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<td>Outcome:</td>
<td>07 Nutritional Status</td>
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<td>Study</td>
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<td>Control Mean (SD)</td>
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<td>Weight</td>
<td>WMD (fixed) 95% CI</td>
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<td>01 Study:</td>
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<tr>
<td>Rabeneck 1998</td>
<td>39</td>
<td>-0.10 (3.97)</td>
<td>39</td>
<td>-0.10 (2.90)</td>
<td>66.32</td>
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<tr>
<td>Schwenk 1999</td>
<td>26</td>
<td>1.60 (5.20)</td>
<td>26</td>
<td>2.70 (7.40)</td>
<td>1.12</td>
<td>-0.10 [-7.62, 7.42]</td>
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<tr>
<td>De Luis 2003</td>
<td>38</td>
<td>1.60 (5.77)</td>
<td>38</td>
<td>0.90 (1.89)</td>
<td>12.33</td>
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<td>Subtotal (95% CI)</td>
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<td></td>
<td>100.00</td>
<td>0.29 [-0.31, 1.09]</td>
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<tr>
<td>Test for heterogeneity: Ch² = 1.08, df = 2 (P = 0.58), η² = 0%</td>
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<td>Test for overall effect: Z = 0.72 (P = 0.47)</td>
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<tr>
<td>02 Lean Body Mass</td>
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<tr>
<td>Rabeneck 1998</td>
<td>39</td>
<td>0.20 (4.60)</td>
<td>39</td>
<td>0.00 (3.07)</td>
<td>92.12</td>
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<tr>
<td>Schwenk 1999</td>
<td>26</td>
<td>1.60 (4.50)</td>
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<td>3.00 (6.20)</td>
<td>17.88</td>
<td>-2.20 [-6.22, 0.82]</td>
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<td>De Luis 2003</td>
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<td>-0.20 (0.00)</td>
<td>38</td>
<td>0.20 (0.00)</td>
<td>100.00</td>
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<td>Subtotal (95% CI)</td>
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<td>03 Body Fat</td>
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<td>Rabeneck 1998</td>
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<td>0.40 (2.88)</td>
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<td>1.00 (6.50)</td>
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<td>3.60 (4.00)</td>
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<td>1.30 (2.73)</td>
<td>36</td>
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APPENDIX 3 META-ANALYSIS PLOTS

Figure 1: Changes from baseline in nutritional status
Figure 2: Changes from baseline in dietary intake

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Treatment Mean (SD)</th>
<th>Control Mean (SD)</th>
<th>WMD (fixed) 95% CI</th>
<th>Weight %</th>
<th>WMD (fixed) 95% CI</th>
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<td>24</td>
<td>9.00 (10.81)</td>
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<td>De Luis 2002</td>
<td>36</td>
<td>6.30 (13.31)</td>
<td>1.00 (2.09)</td>
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<tr>
<td>Subtotal (95% CI)</td>
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<td>02 Protein</td>
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<td>Subtotal (95% CI)</td>
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<td>03 Fat</td>
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<td>Subtotal (95% CI)</td>
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<tr>
<td>Test for overall effect: not applicable</td>
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Not estimable