



## Interventions for fatigue and weight loss in adults with advanced progressive illness

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# Interventions for fatigue and weight loss in adults with advanced progressive illness

## Review information

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### History

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## Abstract

### Background

### Objectives

### Methods

### Main results

### Authors' conclusions

## Plain language summary

[Summary title]

[Summary text]

## Background

### Description of the condition

For the purposes of this overview advanced progressive illnesses are defined as conditions for which there is no cure and which have significant morbidity in the latter stages of illness. These conditions include degenerative neurological conditions, irreversible organ failure, widespread malignant disease and acquired immune deficiency

syndrome (AIDS). The underlying medical condition can affect both the speed of functional decline and the potential for health improvements with appropriate interventions ([Davies 2004](#)). Pain, anxiety and depression are also common symptoms within advanced illness but are not the focus of this review.

Fatigue and unintentional weight loss are two of the commonest symptoms experienced by people with advanced progressive illness ([Brunnhuber 2008](#); [Davis 2000](#); [Solano 2006](#)) and can be of great concern to those affected and of even greater concern to formal and informal caregivers ([Hopkinson 2006](#); [Poole 2002](#); [Reid 2009](#)). Altered metabolism, inadequate intake of nutrients, muscle deconditioning and poor energy management have all been implicated in the development and exacerbation of these symptoms ([Carey 2000](#); [MacDonald 2007](#); [Radbruch 2008](#)).

### **Fatigue**

"Fatigue is a subjective, unpleasant symptom which incorporates total feelings ranging from tiredness to exhaustion creating an unrelenting overall condition which interferes with individuals' ability to function to their normal capacity." ([Ream 1996](#)). Fatigue is a common complaint within general populations, however, it is the severe and unrelenting nature of fatigue in advanced progressive illness which negatively impacts on physical, psychological, social and spiritual well-being ([Pederson 2003](#); [Potter 2004](#); [Purcell 2009](#)). As a symptom fatigue is often overlooked and under diagnosed, and seen as an inevitable consequence of deteriorating health ([Toye 2006](#); [Whitehead 2009](#)). Reduced activity in response to fatigue can lead to further muscle deconditioning which can exacerbate the symptom ([Ream 2007](#)).

### **Unintentional weight loss**

Significant unintentional weight loss, nominally defined as loss greater than 10% of usual body weight, is an independent indicator of poor prognosis in chronic illness ([Norman 2008](#)). Control of unintentional weight loss in people with advanced progressive illness is difficult as changes in metabolic rate and in the processing of nutrients for energy may mean that predictive equations are unrepresentative of patient macro and micronutrient needs ([Caro 2007](#)). Persistent weight loss in the presence of adequate nutrition as determined by predictive equations is known as anorexia cachexia syndrome (ACS) ([Carey 2000](#); [MacDonald 2007](#)). Weight loss from ACS is not the same as weight loss during starvation. A healthy person's body can adjust to starvation by slowing down its use of nutrients, but in patients with ACS, the body does not make this adjustment. Therefore weight loss in patients with ACS is unlikely to be reversed simply by eating more or by the provision of supplementary artificial feeding ([Caro 2007](#); [Evans 2008](#); [MacDonald 2003](#); [MacDonald 2007](#)).

The main symptoms of weight loss from ACS are:

- severe loss of weight, including loss of muscle with or without loss of fat mass,
- loss of appetite,
- feeling sick (nausea),
- feeling full after eating small amounts (early satiety),
- anaemia (low red blood cell count),
- weakness and fatigue ([Carey 2000](#); [Evans 2008](#)).

Unintentional weight loss can result from reduced nutrient intake, improper nutrient utilisation and activation of biochemical processes which induce catabolism ([Carey 2000](#); [Evans 2008](#)). Factors which may reduce nutrient intake include:

- physical discomfort from uncontrolled pain, bloating, reflux or nausea;
- poor appetite or early satiety due to delayed gastric emptying, slowed gastrointestinal transit or ascites;
- oral problems including a sore or dry mouth, taste changes, infection, poor dentition or ill fitting dentures;
- side effects from prescribed or over the counter medications;
- adherence to a therapeutic or altered consistency diet or suffering from food aversions which limit food choice;
- reliance on others to buy or prepare food or to assist with feeding;
- depression or anxiety caused by loss of hope, spiritual distress or loss of social status and social contact;
- breathlessness and fatigue;
- influences of culture, family and other belief systems ([Alibhai 2005](#); [Aston 2006](#); [Richardson 2004](#)).

Factors which may affect nutrient utilisation include:

- presence of fistulae involving the gastrointestinal tract;
- nutrient malabsorption due to diarrhoea, drug-nutrient interaction or enzyme depletion;
- muscle atrophy as a consequence of reduced contractile work ([Carey 2000](#); [Evans 2008](#)).

Fatigue and unintentional weight loss can therefore affect the physical, psychological, social and cognitive functioning of a patient.

- Physical: tiredness, weakness, malaise, lack of energy, lethargy, exhaustion, aching body, dyspnoea.
- Psychological and social: lack of motivation, anxiety, sadness, depression, low self esteem.
- Cognitive: inability to concentrate, lack of attention, poor memory, difficulty thinking and impaired decision making ([Benzein 2005](#); [Hinsley 2007](#); [Poole 2002](#); [Ream 2007](#)).

The majority of health care professionals working in hospitals, primary care facilities and the community will care

for people with advanced progressive illness where the intent of any intervention is palliative (Davies 2004). Palliative care is defined by the World Health Organization as "an approach that improves the quality of life of clients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual." (WHO 2002). Palliative services have been mainly developed through the observation and treatment of people with cancer related symptoms (NCPC 2002; NICE 2004). There is now recognition of the need to extend and apply this approach to anyone suffering from uncontrolled symptoms of advanced progressive illness (NCPC 2005).

The National Council for Palliative Care state that interventions to control symptoms such as fatigue and unintentional weight loss can bring considerable improvements in function and quality of life to seriously ill people and their families, reducing physical, psychological and spiritual distress (NCPC 2000).

## Description of the interventions

Any intervention primarily aimed at the management of fatigue and unintentional weight loss in advanced progressive illness will be included. Interventions may include exercise, behavioural management, use of assistive devices, lifestyle management, nutritional support, pharmacological interventions, complementary or alternative therapy and counselling.

## How the intervention might work

The mechanism of action for included interventions will be through primary and secondary intervention strategies.

Primary intervention strategies for fatigue may help preserve muscle mass and maintain energy reserves through interventions such as exercise, activity pacing, relaxation and support services.

For unintentional weight loss primary intervention strategies may help preserve body weight through interventions such as nutritional supplementation to produce positive energy balance, weight bearing exercise to increase lean body mass, pharmacological agents to down-regulate inflammatory processes and improve nitrogen balance and psychological and social interventions that increase desire to eat.

Secondary intervention strategies may include strategies to adapt to functional decline and weight loss rather than seeking to alleviate them, such as counselling and complementary therapy support.

## Why it is important to do this overview

Many studies have looked at ameliorating fatigue and unintentional weight loss through pharmacological and non pharmacological means. Systematic reviews have been conducted looking at interventions using single modalities such as exercise, nutrition, drug therapy, complementary or alternative medicine or psychosocial interventions.

This work will gather together data from a wide range of reviews into one overview. This overview will be of benefit to clinicians, policy makers and informed consumers who are accessing *The Cochrane Library* for evidence on treatments of fatigue and unintentional weight loss in adults with advanced progressive illness. Data from this overview will be used to highlight areas needing further research.

## Objectives

To review evidence to determine the efficacy of interventions used in the management of fatigue and/or unintentional weight loss in adults with advanced progressive illness by reviewing the evidence contained within Cochrane reviews.

## Methods

### Criteria for considering reviews for inclusion

All Cochrane reviews that assessed the effects of an intervention on fatigue and/or unintentional weight loss in adults with advanced progressive illness will be included in the overview. Systematic reviews published outside *The Cochrane Library* will not be included.

### Search methods for identification of reviews

Searching by identified key word or subject heading would be unreliable due to the diverse range of interventions and illnesses under review. The Cochrane Database of Systematic Reviews will be handsearched by title for all reviews that may assess the effect of an intervention on fatigue and/or unintentional weight loss in adults with advanced progressive illness. Titles of interest will be further reviewed by abstract. Where the relevance of a study is under question the full review will be handsearched for types of participant and relevance of outcome measures and a consensus opinion reached.

### Types of studies

Cochrane systematic reviews of interventions with fatigue and/or unintentional weight loss as primary treatment intent will be included.

### Types of participants

Adults 18 years or older, with an advanced progressive illness which is known to have clinically significant fatigue and/or weight loss in the latter stages of illness. These conditions include degenerative neurological conditions, such as Multiple Sclerosis, Parkinsons Disease and Dementia, irreversible organ failure, widespread malignant disease and acquired immune deficiency syndrome (AIDS).

### ***Types of outcome measure***

Primary outcomes:

1. Clinically significant improvements in fatigue and/or unintentional weight loss.
2. Improvements in quality of life of people who have fatigue and/or unintentional weight loss.
3. Withdrawals due to adverse events.

### **Data collection and analysis**

#### ***Selection of reviews***

The selection criteria will be applied to reviews by two overview authors, independently. Reviews studying interventions with fatigue and/or unintentional weight loss as primary treatment intent will be included. Reviews identifying interventions impacting on fatigue and/or unintentional weight loss in advanced progressive illness, where the treatment of these symptoms was not the primary indication for the intervention will be listed within excluded studies. Disagreements will be resolved through discussion. If necessary, authors will seek additional information from the authors of included systematic reviews or from authors of primary studies included within the systematic reviews.

#### ***Data extraction and management***

The data will be extracted independently by two overview authors using a data extraction form. Where there are disagreements this will be arbitrated by the third overview author and a majority decision reached. The data extraction form will summarise key characteristics of the review including the objectives, information on participants, interventions examined, outcomes assessed and comparisons performed. In some instances, data may be transformed to make them consistent with other analyses. The data will be grouped according to condition, intervention and/or symptom as appropriate.

#### ***Assessment of methodological quality of included reviews***

Two different quality assessments will be addressed by the Overview authors: the methodological quality of reviews summarised in the Overview and the quality of the evidence in these reviews using predefined criteria. Where a Cochrane Review contains a risk of bias table this will be used. If there is no risk of bias table we will use AMSTAR to assess the methodological quality of the review ([Shea 2007](#)). We will attempt to use the GRADE approach ([GRADE Working Group 2004](#)) to assess the quality of evidence across studies for each important outcome. Two overview authors will apply the criteria independently. Where there are disagreements this will be arbitrated by the third overview author and a consensus reached.

#### ***Data synthesis***

This overview will present findings from systematic reviews on interventions to manage fatigue and unintentional weight loss in adults with advanced progressive illness and direct readers to the individual systematic reviews for additional detail. Any important limitations of data or data analyses will be stated.

Where possible, data will be extracted from the included systematic reviews and presented in table or figure format. The overview may include indirect comparisons based on formal statistical analyses, especially if there is no evidence on direct comparisons. Indirect comparisons will not be performed where it is believed that studies using direct comparisons have been performed.

## **Results**

### **Description of included reviews**

### **Methodological quality of included reviews**

### **Effects of interventions**

## **Discussion**

### **Summary of main results**

### **Overall completeness and applicability of evidence**

### **Quality of the evidence**

### **Potential biases in the overview process**

### **Agreements and disagreements with other studies or reviews**

## **Authors' conclusions**

### **Implications for practice**

## Implications for research

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## Contributions of authors

Cathy Payne conceived and coordinated the overview. Funding was secured by Cathy Payne. All authors will contribute to data extraction, i.e. Cathy Payne, Suzanne Martin, and Phil Wiffen. All authors will contribute toward the writing of the overview.

## Declarations of interest

There are no conflicts of interest with this review for Cathy Payne, Suzanne Martin or Philip J Wiffen.

## Differences between protocol and review

## Published notes

## Additional tables

## References to reviews

### Included reviews

### Excluded reviews

## Other references

### Additional references

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## **Other published versions of this review**

### **Classification pending references**

## **Figures**

## **Sources of support**

### **Internal sources**

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### **External sources**

- No sources of support provided

## **Feedback**

## **Appendices**