

# Prevalence, incidence and clinical impact of cachexia: facts and numbers—update 2014

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**Abstract** Cachexia is a serious but underrecognised consequence of many chronic diseases. Its prevalence ranges from 5–15 % in end-stage chronic heart failure to 50–80 % in advanced cancer. Cachexia is also part of the terminal course of many patients with chronic kidney disease, chronic obstructive pulmonary disease (COPD) and rheumatoid arthritis. Mortality rates of patients with cachexia range from 10–15 % per year in COPD through 20–30 % per year in chronic heart failure and chronic kidney disease to 80 % in cancer. The condition is also associated with poor quality of life. In the industrialised world, the overall prevalence of cachexia (due to any disease and not necessarily associated with hospital admission) is growing and it currently affects around 1 % of the patient population, i.e. around 9 million people. It is also a significant health problem in other parts of the globe. Recently there have been advances in our understanding of the multifactorial nature of the condition, and particularly of the role of inflammatory mediators and the imbalance of anabolism and catabolism. Several promising approaches to treatment have failed to live up to the challenge of phase III clinical trials, but the ghrelin receptor agonist anamorelin seems to have fulfilled at least some early promise. Further advances are urgently needed.

**Keywords** Cachexia · Wasting · Prevalence · Epidemiology · Treatment

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Cachexia is a serious but underrecognised consequence of many chronic diseases. Its prevalence is 5–15 % in end-stage chronic heart failure (HF) and it forms part of the terminal course of many patients with chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD) and rheumatoid arthritis. However, cachexia is associated particularly with cancer. Using data from the Nationwide Inpatient Sample, Arthur et al. recently estimated the annual prevalence of cachexia admissions to community hospitals in the USA at over 160,000 cases [1]. The median duration of stay was 6 days, compared with 3 days for non-cachexia admissions, at a median cost of more than 10,000 dollars per case (4000 dollars more than for non-cachexia patients). Cachexia patients also experienced greater loss of function than those admitted with other diagnoses [1]. This gives a partial picture of the burden this condition imposes both on patients and on healthcare systems. Globally, the overall prevalence of cachexia (due to any disease and not necessarily leading to hospital admission) is around 1 % of the patient population, i.e. around 9 million people are affected [2]. Argiles et al. estimated that cachexia affects 50–80 % of cancer patients and accounts for up to 20 % of cancer deaths [3]. Indeed, death normally ensues when weight loss exceeds 30–40 % [1]. However, many other patients (perhaps 50 %) die with but not of cachexia. Table 1 gives an estimate of the prevalence of cachexia in various chronic illnesses.

Mortality rates of patients with cachexia range from 10 to 15 % per year in COPD through 20–30 % per year in chronic HF and CKD to 80 % in cancer. The condition is also associated with poor quality of life. Indeed, cachexia was eloquently described already by Hippocrates as an invariably fatal disease in which “the flesh is consumed and becomes water” [4]. It is evoked equally chillingly by Herta Müller, winner of the 2009 Nobel Prize in Literature, who wrote that “once the flesh has disappeared from the body, carrying the bones becomes a burden; it draws you down into the earth [5]”.

**Table 1** Estimated clinical impact of cachexia in different chronic illnesses in Europe in 2014. Estimates are assumed to be rather conservative

	Prevalence of illness in population (%)	Patients at risk (%)	Prevalence in patients at risk (%)	Absolute number of patients with cachexia <sup>a</sup>	1-year mortality of patients with cachexia (%)
COPD, moderate	3.5	15	35	1.4 m	15–25
Chronic HF, NYHA II–IV	2.0	80	10	1.2 m	20–40
Cancer, all types	0.5	90	30	1.0 m	20–60
Rheumatoid arthritis, severe	0.8	20	10	120,000	5
End-stage chronic kidney disease	0.1	50	50	185,000	20

<sup>a</sup> Assumptions are based on a total population of 742 million in Europe. By comparison, the assumed population of the US is 300 million, and of Japan 100 million

A number of treatments have been suggested for cachexia; however, therapies for the underlying illness remain at the forefront and no direct treatment of cachexia is available as yet. This is true despite the fact that PubMed citations of journal articles relevant to cachexia almost doubled in the decade 2003 to 2013. Even so, global awareness of the importance of cachexia, particularly on web pages accessible to the public and on those presenting the guidelines of oncology and other specialist societies, remains low [6].

Overall, our understanding of the pathophysiology of cachexia has made some progress in recent years and, therefore, some studies have been published with promising results. In a recent trial, conducted in patients aged 70 years and older receiving chemotherapy for solid tumours and at risk of malnutrition, dietary counselling increased calorie and protein intake relative to a control group managed by usual care [7]. However, mortality was not reduced in the intervention group and response to chemotherapy was not improved. This outcome confirms the view that the adverse effects of cachexia cannot be addressed by additional nutrition alone and supports the hypothesis that the condition involves activation of an inflammatory response and an imbalance between anabolism and catabolism, leading to selective wasting of muscle.

Cachexia is also common in advanced HF, and there has been recent interest in the role of right ventricular dysfunction, which correlates with weight loss. In these HF patients, wasting of fat but not of lean mass predicted adverse outcome [8]; skeletal muscle wasting, however, was associated with low exercise capacity and low functional status [9, 10]. In cancer, however, it is depletion of skeletal muscle that has been linked to poor prognosis, independently of body mass index [11].

The precise criteria employed to define cachexia by different research groups vary, and this can have major implications for its reported prevalence. We prefer to define cachexia as suggested in Table 2. Wallengren et al. found recently that the proportion of palliative care cancer patients classified as being cachectic ranged from 12 to 85 % depending on the definition used [13]. Elements common to the way cachexia is defined include weight loss, low body mass index, fatigue, and biochemical markers of systemic inflammation. As mentioned

above, a key concept is that while malnutrition is reversible when adequate amounts of food are provided, cachexia is not. But, however it is defined, involuntary weight loss in patients reaching the terminal phase of many chronic diseases is common and severe enough to constitute a public health problem [14]. Cachexia amply meets all the necessary criteria: it is a major contributor to morbidity and mortality, to impaired quality of life and to healthcare costs.

Among patients with cachexia, or at risk of developing it, we urgently need treatments that will enhance muscle mass or at least slow its depletion, maintain body weight, improve strength, enhance the capacity for independent functioning, and prolong survival. It is a feature of trials of potentially effective agents that the number of patients involved is generally small and that most studies are confined to patients with cancer-related cachexia [15]. Among appetite stimulants, megestrol acetate and L-carnitine have shown recent promise, while melatonin has not. Trials of anti-inflammatories published over the past 2 years have generally been disappointing. In 2013, two placebo-controlled phase III trials of the oral ghrelin receptor agonist anamorelin were reported, as well as two phase III trials of the selective androgen receptor modulator enobosarm. All four trials were conducted in patients with cancer, but neither trial program met all its combined primary endpoints.

**Table 2** Diagnostic criteria for cachexia. Adapted from [12]

1. Presence of a chronic disease <i>AND</i>
2. Loss of body weight $\geq 5$ % within the previous 12 months or less <i>AND</i>
3. Presence of at least three of the following
- Reduced muscle strength
- Fatigue
- Anorexia
- Low fat-free mass index
- Abnormal biochemistry
- Inflammation
- Anaemia
- Low albumin

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