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Cachexia as a major public health problem: frequent, costly, and deadly

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Abstract Perception of healthy body size and composition differs considerably across the globe, ethnic groups, cultures, and even inside medical community. Although the concept of ideal body weight has evolved over the past decades, the observation that weight loss can have more deleterious effects within a short-term period than weight gain has remained rather consistent. Weight loss, as a prelude to cachexia, occurs frequently in a variety of disease states and meets the requirements of a global public health problem. Consequently, interventions to prevent and control chronic diseases require a comprehensive approach that targets a population as a whole and includes both prevention and treatment strategies. Around the globe, cachexia awareness campaigns and expanding the current public health priorities to highlight the cachexia magnitude and areas of

interventions is necessary. Simultaneously, scientific efforts should provide us with more reliable estimates of body wasting and cachexia as well as pathophysiology of cachexia-associated death. As certain proportion of patients will, irrespective of preventive measures, eventually develop cachexia, a quest for effective remedy remains vital.

Keywords Cachexia · Chronic disease · Prevention · Public health

1 Introduction

Perception of healthy body size and composition differs considerably across the globe, ethnic groups, cultures, and even inside medical community. During lifetime, most individuals experience weight reduction due to many reasons. The world is primarily aware of malnutrition consequences. These clearly represent a major health problem worldwide with over a billion persons, mostly women and children, suffering from hunger. More persons die from hunger each year than AIDS, malaria, and tuberculosis combined. However, in the developed world and much of the developing world disease-related weight loss, which is assuming epidemic proportions, is frequently ignored. Body wasting and cachexia, however, can develop in a variety of acute and chronic conditions to be associated with grim outcome [1, 2]. These include infectious diseases, such as HIV/AIDS, malaria, and tuberculosis, as well as many chronic conditions like cancer, chronic heart failure (CHF), chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), cystic fibrosis, liver cirrhosis, Crohn's disease, rheumatoid arthritis, stroke, and neurological degenerative disease [3–5]. Cachexia has also been noted in patients after extensive traumatic injury and sepsis [1, 2].

The prevalence of an illness or condition is defined as the number of individuals who have the condition at any

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Table 1 Prevalence (in millions) of selected conditions by World Health Organization region, 2004

Condition (millions)	World	Europe	Africa	Americas	South-East Asia	Western Pacific	Eastern Mediterranean
Tuberculosis	13.9	0.6	3.0	0.5	5.0	3.8	1.1
HIV infection	31.4	2.0	21.7	2.8	3.3	1.0	0.5
Stroke survivors	30.7	9.6	1.6	4.8	4.5	9.1	1.1
COPD	63.6	11.3	1.5	13.2	13.9	20.2	3.3
Rheumatoid arthritis	23.7	6.2	1.2	4.6	4.4	6.0	1.3

Modified from [6]

HIV human immunodeficiency virus, *COPD* chronic obstructive pulmonary disease

moment [6]. Exact prevalence of cachexia-associated conditions is essential to assess cachexia prevalence. Table 1 summarizes the prevalence of various conditions from World Health Organization (WHO) regions [6]. Several relevant diseases that can lead to cachexia are not included in this report thus worldwide estimation of cachexia burden remains inconclusive [1, 7]. We therefore often have to rely on fragmented data from individual countries [8, 9] or on several studies focusing on various conditions [1] (Table 2). Unfortunately, the estimate is only as good as the available data. Across the existing literature, several definitions and different populations have been evaluated. With recent cachexia definition [10] from the Cachexia Consensus Working Group at hand (Fig. 1), more reliable data about cachexia should be available in the next years [11]. With new data at hand, past estimates may need adjustment and prevalence of cachexia is likely to increase [1].

2 Epidemiological considerations

Misconceptions about cachexia, even in medical and scientific community, are many. Terms as “cachexia,” “malnutrition,” “anorexia,” and “sarcopenia” are frequently used as synonyms although they relate to completely different conditions [4]. With regard to topic of this article, malnutrition needs particular attention. It is frequent around the world and represents a

major issue for developing countries and community as a whole. However, it can be reversed by simple refeeding whereas such a strategy alone is ineffective in cachexia. On the other hand, in developing countries malnutrition is, if present sufficiently long and particularly in combination with rheumatic heart disease or Chagas disease, a major contributor to CHF and increased risk to develop cachexia [2].

A recent estimate suggests that approximately nine million patients have cachexia of chronic disease, with the highest prevalence (currently about 1 %) being recorded in North America, Europe, and Japan [1]. Given the population size in Asia, it is very likely that the worldwide burden of cachexia will continue to escalate. The data for Africa and South America are scarce, although reports on cardiovascular disease [12–14] suggest that epidemiological transition has broadened the spectrum of cachexia aetiology in these regions.

Different figures have been reported for prevalence of cachexia in individual conditions; yet, common belief is that

CHRONIC CONDITION WITH:

≥5% weight loss in <12 months

OR

body mass index <20kg/m²

+

3 OUT OF 5 ADDITIONAL CRITERIA:

- fatigue
- decreased muscle strength
- anorexia
- low fat-free index
- abnormal biochemistry
 - anaemia (<120g/L)
 - low serum albumin (<32g/L)
 - increased inflammatory markers
 - CRP >5mg/L
 - IL-6 >4pg/mL

Table 2 Prevalence (in percent) of cachexia in some diseases

Disease	Prevalence (%)
Cancer	28–57
Chronic heart failure	16–42
Chronic kidney disease	30–60
COPD	27–35
Rheumatoid arthritis	18–67
HIV/AIDS	10–35

Modified from [1, 8]

COPD chronic obstructive pulmonary disease, *HIV/AIDS* human immunodeficiency virus/acquired immunodeficiency syndrome

Fig. 1 Cachexia definition from the Cachexia Consensus Working Group. Modified from [10]

patients with advanced conditions, particularly cancer, are more prone to develop cachexia (Table 2). In terms of absolute numbers, conditions with high population burden like COPD and CHF cachexia take the lead.

Cachexia increases mortality in chronic disease and is present in about 30 % of patients that die. Annual mortality rates are disease dependent: COPD, 10–15 % and CHF or CKD, 20–30 % [1]. An exponential increase to 80 % in cancer translates to two million cancer-related cachexia deaths, i.e., about every second patient with malignant disease will die with some degree of cachexia [15]. From this point of view, cachexia is not merely a complex syndrome that occurs in advanced stages of various chronic diseases but one of the major killers worldwide.

3 Is cachexia a public health problem?

The ultimate goal of public health has always been and remains the prevention of disease and the promotion of health in communities [16]. In contrast to clinical medicine, public health addresses population groups rather than single individuals and acts through comprehensive and multisectoral interventions. Whereas target diseases and risk factors are largely shared with clinical medicine, public health aims to prevent development of clinically relevant or even full-blown disease to reduce the burden for population and healthcare system. Although no mandatory definition of public health problem is accepted, some general guidance is adopted in the scientific community. For a health condition to be considered as a public health problem, at least four characteristics should be present (Fig. 2). Firstly, the condition burden is high in terms of morbidity, mortality, quality of life, and costs. Secondly, the problem is distributed unfairly, affecting disadvantaged population groups to a greater extent. Thirdly, there

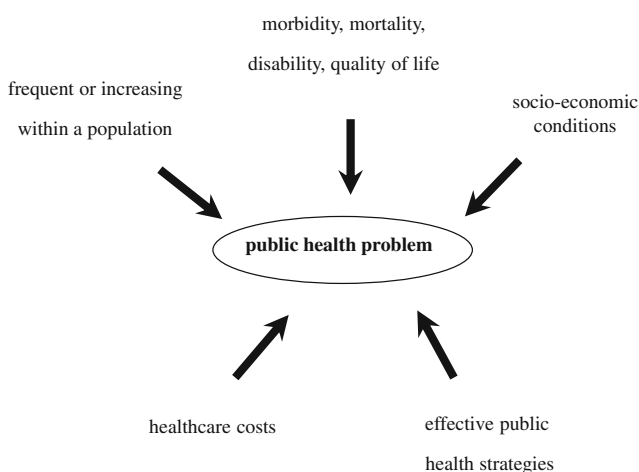


Fig. 2 Characteristics of a public health problem

must be some evidence that public health strategies could substantially reduce the burden of the condition. Lastly, such preventive strategies are not yet fully in place [17, 18]. Next to the epidemiological and causation background [19], maybe the most important requirement should be the feasibility of relatively simple and cost-effective population-wide strategies to reverse the natural course of the condition [20].

Although many people still believe that chronic diseases are problems of developed communities who have acquired them primarily through indulging in four preventable behaviors (insufficient physical activity, tobacco use, unhealthy diet, and the harmful use of alcohol) [21], the situation around the globe has already started to change [12, 20, 22, 23]. Based on the latest WHO Global Status Report on Non-communicable Diseases, it is estimated that out of 57 million global deaths in 2008, 36 million (63 %) were due to chronic diseases, principally cardiovascular diseases, diabetes, cancers, and chronic respiratory diseases [20]. Nearly 80 % (29 million) of chronic disease deaths occur in the developing world: about 80 % of cardiovascular and diabetes deaths, 90 % of COPD deaths, and about two thirds of cancer deaths. Importantly, in low- and middle-income countries deaths from chronic diseases occur at younger age that hampers social and economic development [20, 24]. As chronic diseases have already started to dominate global public health [24], low- and middle-income countries are facing a double burden of disease. While they continue to deal with the problems of infectious diseases, they are experiencing a rapid upsurge in chronic disease risk factors and deaths, especially in urban settings [25]. Over last decades, we have witnessed dramatic changes in eating, drinking, and moving habits around the globe. Generally, these now clash with our biology and physiology to cause major shifts in body size and composition [26]. The body mass index had a constant trend of increase by 0.4 kg/m² per decade thus doubling the worldwide obesity and overweight prevalence from 1980 to 2008 [27, 28]. Importantly, this increase occurred in an accelerated fashion with half of the rise occurring in 1980 to 2000 and half in only 8 years from 2000 to 2008 [28]. There is some variation in levels and trends [27–29] but generally speaking, the increase is more pronounced in low and middle income countries [30]. Similarly, the prevalence of hypertension is increasing in developing countries with the current prevalence of 16–37 %, and increases of up to 30 % in last decades [31]. This eventually translates into double burden of disease as these countries are facing an epidemic of chronic diseases through increasing prevalence of risk factors [32]. Indeed, the risk factor associated population attributable fractions of fatal coronary heart disease and stroke indicate further increase in double burden with the growing potential for wasting and cachexia associated with chronic disease [30].

Taking different projections of global mortality and disease burden into account, the world will experience further

shift in the distribution of deaths from younger to older age groups and from infectious to chronic diseases during next decades. Large declines in mortality are projected to occur between 2002 and 2030 for all of the principle communicable, maternal, perinatal, and nutritional causes, with the exception of HIV/AIDS. The four leading causes of death globally in 2030 will be ischemic heart disease, stroke, COPD and HIV/AIDS [33].

Based on epidemiological data and public health problem characteristics, we are proponents of qualifying cachexia as a global public health problem. This should in our opinion increase the awareness about cachexia and help the community to comprehend its complexity and magnitude.

4 Management strategies

Cardiovascular disease, cancer, diabetes, and chronic respiratory diseases are both most prevalent and largely preventable conditions. Population-wide interventions to prevent chronic disease are feasible at low-cost which gives ample opportunities even in countries with low income levels. Bringing this to a higher level, WHO considers some interventions as “best buys” when immediate actions should be undertaken to produce accelerated results in terms of lives saved, diseases prevented, and heavy costs avoided (Table 3) [20]. For those at high risk or with chronic disease, an alternate approach through individual healthcare interventions is necessary.

Evidence from high-income countries shows that a focus on both prevention and improved treatment following cardiovascular events led to dramatic declines in mortality rates. Similarly, progress in cancer treatment combined with early detection and screening have improved survival rates for many cancers. As these approaches address risk factors and progression of disease, respectively, population-wide approach has to be complemented by individual healthcare interventions [20]. Effective preventive strategies to tackle socio-economic inequalities, malnutrition, infectious disease, and modern community-related conditions will merely shift the burden towards refractory chronic disease stage with significant potential to increase cachexia burden.

Future management, provided that preventive strategies are implemented and successful, will therefore critically depend upon potent remedy against cachexia (not available yet) and supportive measures to meet needs of dependent patients (currently not affordable by any community). In other words, we may experience a transition of cachexia aetiology rather than a story of success. Therefore, a joined perspective of public health practitioners and clinicians about issues dealing with cachexia should be initiated. Meanwhile, intense efforts to find treatment for cachexia should be maintained [34]. To identify suitable patients, a reliable and routine marker reflecting therapeutic target (muscle mass in this case) would be preferred, and creatinine appears as an attractive option [35].

Public and medical community awareness about cachexia should be a primary target for future interventions. This could enhance detection of individuals at risk of or those with body wasting and pre-cachexia. Around the globe, target populations and interventions may differ. Socio-economic inequalities like poverty, level of education, housing and type of occupation are in an independent manner associated with risk factors, disease progression and outcome. As a key and maybe even a rate limiting step in disease’s natural course, they require multisectoral and comprehensive measures, which to a great extent are beyond the scope of medicine alone. Accessibility to healthcare system and basic level of drug availability remain an issue at large. Unmanaged chronic conditions can therefore easily and more quickly develop into full-blown disease and eventually cachexia. After several trials with pharmacological interventions in chronic disease, including the polypill in cardiovascular disease [36], such an approach is promoted over standard public health measures. The jury about this disputed topic, however, is still out and additional research is warranted before accepting such an approach as first line management.

5 Conclusions and future research

Identifying condition as a public health problem often serves implicit normative or political purposes [19]. Yet, in case of

Table 3 Examples of “best buys” according to World Health Organization

Population-wide interventions	Individual healthcare interventions
Bans: on smoking in public places and on tobacco and alcohol advertising	Aspirin, statin, and blood pressure-lowering agents for people at high cardiovascular risk
Raising taxes: on tobacco and alcohol	Administration of aspirin to people who develop a myocardial infarction
Raising public awareness: about diet and physical activity	Blood pressure, glycemic control, and foot care for patients with diabetes
Vaccination: against hepatitis B and human papilloma virus	

Modified from [20]

cachexia this is true reflection of epidemiological and clinical circumstances, which has not been acknowledged neither by the community nor by the medical care professionals. We have to perceive the dynamic course of body weight through lifespan where weight loss can have more deleterious effects than weight gain [37, 38]. This should in our opinion increase the awareness about cachexia and help the community to comprehend its complexity and magnitude.

Action to prevent and control chronic diseases requires a comprehensive approach that targets a population as a whole and includes both prevention and treatment interventions. It has to be multisectorial with collaboration efforts from government, international organizations, academic institutions, civil society and the private sector [39]. Around the globe, a shift in current public health priorities to highlight the magnitude of the problem and areas of interventions is necessary. Simultaneously, scientific efforts should provide us with more reliable estimates of body wasting and cachexia as well as pathophysiology of cachexia-associated death. As a certain proportion of patients will, irrespective of preventive measures, eventually develop cachexia, a quest for effective remedies remains vital.

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