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Nutrition In General Practice

Caroline A.M. van Wayenburg

Nutrition In General Practice

Box 1: Explanation of the terminology used in the main text, due to the lack of universal definitions

Cachexia (syndrome):

A hyper-metabolic condition due to systemic inflammatory processes, or other (yet unravelled) disease related pathological changes, resulting in the loss of mainly muscle mass ((often) objectified by weight loss), anorexia and weakness.⁴⁻⁹

Malnutrition:

The scientific definition includes both the deficiency or excess (or imbalance) of energy, protein and other nutrients.¹⁰

Nutritional deficiency:

The deficiency of a single micronutrient up to multiple (macro-) nutrients, which incorporates e.g. cachexia, nutritional depletion, nutritional impairment, sarcopenia, undernutrition and wasting.

Nutritional depletion:

See undernutrition, in a gradual deterioration process (this depends on the (multi-) causal pathology).

Nutritional impairment:

See undernutrition, in an acute or more gradual deterioration process (this depends on the (multi-) causal pathology).

Sarcopenia:

Physiological loss of muscle mass due to ageing influenced by health status, physical activity and possibly diet.^{11;12}

Undernutrition/undernourishment:

A nutritional status resulted from a negative balance of energy, protein or other nutrients, leading to measurable adverse effects on tissue/body shape/size/composition (e.g. weight loss, low Body Mass Index (BMI)), function and clinical outcome.¹⁰

Wasting/Emaciation:

Physiological loss of both muscle and fat mass by starvation.

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Caroline A.M. van Wayenburg

This thesis has been prepared by the Department Primary Care of the Radboud University Nijmegen Medical Centre, the Netherlands. The Department Primary Care participates in the Netherlands School of Primary Care research (CaRe), which has been acknowledged by the Royal Netherlands Academy of Arts and Sciences (KNAW) in 1995.

ISBN/EAN 978-90-9024911-7

Illustrations: Jan Leeuwenburgh

Layout: Martijn Prins

Print: Ipskamp Drukkers

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This thesis was made possible by grants of:

Dutch Dairy Association

Department Primary Care, Radboud University Nijmegen Medical Centre

SBOH, employer of general practitioner trainees



Nutrition In General Practice

Een wetenschappelijke proeve op het gebied van de Medische Wetenschappen

Proefschrift

ter verkrijging van de graad van doctor
aan de Radboud Universiteit Nijmegen
op gezag van de rector magnificus prof. mr. S.C.J.J. Kortmann,
volgens besluit van het college decanen
in het openbaar te verdedigen op woensdag 10 maart 2010
om 15.30 uur precies
door

Caroline Anne Monique van Wayenburg

geboren op 1 maart 1976
te Nijmegen

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“We shall not cease from exploration,
and the end of all our exploring
will be to arrive where we started
and know the place for the first time.”

Uit: *T.S. Eliot, Little Gidding, 1942*

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CHAPTER 1 || 0

Introduction and outline

Introduction

After the Second World War, general practitioners often supplied experience based nutritional prescriptions in daily practice (see for example figure 1). In time, the importance of nutrition in routine practice faded into the background, since prosperity improved food supply, hygiene, and the development of drugs. Nowadays, the side effects of prosperity are evident; the easy access to high energy dense foods served in increasing portion sizes, in combination with a more sedentary life style by motorized vehicles, television and computers, results in an alarming increase of overweight and obesity in the community. On the other hand, prosperity has increased the life-expectancy next to a fertility fall in Western society, and hereby the number of elderly with morbidity continues to rise. These fragile elderly can easily become undernourished. Both undernutrition and overweight/obesity have numerous (health) consequences on community level, but even more on an individual level. Therefore, nutritional management in general practice will become more and more essential. Here the gap between community and patient care can be bridged by universal, selective and indicated prevention (earlier known as primary, secondary and tertiary prevention). Additionally, general practitioners are generally trusted¹ and already consulted for many other problems with a (potential) nutrition component.² In guidelines and other evidence based products, nutrition received only limited attention, as it has been less studied than drugs for their clinical effects. In 1995, nutrition was concerned in 35 of the 53 Dutch College of General Practitioners' guidelines,³ which nowadays increased to 39 of the 83 guidelines.

Figure 1 Nutrition prescription for diarrhoea from a GP* around the year 1950

P. J. M. van Wayenburg, arts Groesbeek - Tel. 08891-1398 Spreekuur: 8-9 en van 1-2 uur van ma. t/m vr., beh. woensdagmiddag R/ _____dag: fris water in de mond opwarmen; warme slappe thee met 1 sacharine tablet (ZONDER suiker of melk) sap van bosbessen ZONDER zoetigheid; maggi bouillon; (bruin) geraspte rauwe appels (gewassen). _____dag en _____dag: tevens drooggekookte rijst. _____Beschuiten (dun boter/jam), karnemelkse pap ZONDER suiker ($\frac{1}{4}$ ltr. karnemelk met 1 eetlepel Nutrix en 1 sacharine tablet) Maggi-bouillon, droge biscuits (Maria) wortelpuree (zonder aardappelen), banaan. _____dag: en _____dag: tevens 4 dunne sneedjes oud brood (dun boter en jam). macaroni, vermicelli } in de Maggi bloem van bloemkool } _____dag: en _____dag: tevens gekookt mager vlees (gehakt of soepvlees) yoghurt, ($\frac{1}{4}$ ltr.), zacht gekookt eitje, pap of pudding van melk ZONDER suiker. _____dag: gewoon mee-eten, MAAR . . . 3 dagen lang nog géén : aardappelen, melk, suiker, vet. Vaak kleine porties (6-8xds.), warm, fijnmaken.

*Paul J.M. van Wayenburg, general practitioner from 1941-1983 in Groesbeek, the Netherlands

Nutrition is just a little part of a disease puzzle. Unhealthy nutrition increases the risk for certain diseases and may negatively influence disease severity or outcome, while adequate nutrition may have positive effects. General practitioners do not have to become nutritionists, but need to have some basic knowledge to provide or initiate proper patient care.

This thesis aims to clarify the importance of nutrition advice for general practitioners in the prevention and treatment of undernutrition and obesity. In introducing this thesis, first the physiological body weight change during life is described in order to come to a better understanding of the background of nutritional deficiency/undernutrition and overweight/obesity. This is followed by the objectives and general outline of this thesis.

Physiological body weight change during life

The human body consists of both fat free (muscle and bone tissue) and fat mass. Muscle mass increases during people's twenties, but after the age of 30 years muscle mass diminishes up to 0.3 kg per year to be over-replaced by fat mainly due to a sedentary life-style. Therefore, body weight peaks to a maximum at the age of 40 to 60 years and stabilizes afterwards. After the age of 70 years body weight diminishes,⁴ mainly due to muscle mass depletion – referred to as sarcopenia.^{11;12}

Over a short period of time, weight fluctuations in a healthy person are narrow. Rosenbaum *et al* showed that the 95% confidence intervals for change in body weight in healthy adults were approximately 2% in one month, 3.5% in three months, 5% in six months and 10% in one year or after up to five years of follow-up.¹³

Nutritional deficiency/undernutrition

In general, the word 'malnutrition' is used to indicate merely undernutrition, although in scientific literature malnutrition also implies overnutrition, as well as deficiencies or imbalances of specific nutrients.¹⁰ Therefore in this thesis, we use the term 'nutritional deficiency' to cover the gliding scale from single micronutrient up to multiple (macro-) nutrient deficiencies. Micronutrients are vitamins, minerals and spore elements and macronutrients comprise carbohydrates, fat and proteins. The more advanced stages of nutritional deficiency are later on often specified by the terms: cachexia, nutritional depletion, nutritional impairment, sarcopenia, undernutrition/undernourishment or wasting/emaciation, depending on the causal and time pathway. These terms are explained in **box 1** on the cover, since universal agreement in definitions are lacking. Eating disorders, such as anorexia nervosa and bulimia nervosa, are out of the scope of this thesis.

Consequences of undernutrition

In general, the consequences of undernutrition range from delayed wound healing,¹⁴ impaired immune function,¹⁵ deterioration of muscle function and above all an increased mortality rate, even independent of the disease severity.¹⁶⁻²⁰ Because of these adverse health effects, undernourished patients have higher consultation and prescription rates in primary care,¹⁸ longer hospital stays^{21;22} and a reduced quality of life.²³⁻²⁵ In the UK, the costs caused by undernutrition have been estimated to be as high as 7.3 billion pounds per year.²⁶ In the Netherlands, this kind of information is not yet available.

Despite this knowledge, high-quality prospective studies on both health effects and the cost effectiveness of early nutritional management in general practice are lacking. In hospitals, the effect of early nutritional management appeared to be economically feasible.^{27;28}

Clinical assessment tools for undernutrition

There is no universal agreement concerning the clinical assessment of undernutrition. According to

the World Health Organization (WHO), a Body Mass Index (BMI) $<18.5 \text{ kg/m}^2$ indicates underweight (table 1),²⁹ which has been based on a higher mortality risk in this group. But for specific groups, different criteria may be required. For patients with Chronic Obstructive Pulmonary Disease (COPD) – who feature in one study of this thesis – a BMI $\leq 21 \text{ kg/m}^2$ has been reported to be an independent predictor of mortality.^{17;30;31} The BMI is used to indicate a more gradual or chronic process of undernutrition, while unintentional weight loss of $\geq 5\%$ in one month or $\geq 10\%$ within half a year is used as a marker for subacute undernutrition. At risk for undernutrition are those patients with unintentional weight loss $\geq 5\%$ but $<10\%$ within half a year.³²

Table 1 BMI classification for Caucasian adults (aged 18-70 years) according to the WHO

BMI (kg/m^2)	Classification
<18.5	Underweight
18.5-24.9	Normal weight
25.0-29.9	Overweight
≥ 30.0	Obesity

In contrast to BMI and weight loss, nutrition screening and assessment questionnaires might trace undernutrition before measurable effects even emerge. Other possible assessment tools in general practice, such as blood samples (e.g. (pre-) albumin), skin-fold thickness or the Bioelectrical Impedance Analysis are still under discussion for their applicability.

Clinical and epidemiological aspects

Nutritional deficiency is a result of an imbalance between nutritional loss, in- or uptake and energy expenditure or a diminished intrinsic production. Examples of the former are: burns, starvation by poverty or social isolation (wasting/emaciation), bad fitting dental prosthesis, loss of appetite, vomiting, diarrhoea or shortage of vitamin D production due to little sunlight exposure. The energy expenditure can be increased by physical activity, fever or other disease related hyper-metabolic changes. This disease inducing ‘cachexia’ has been described in cancer, rheumatic arthritis, COPD, chronic kidney and heart failure patients.³³

In the literature, sarcopenia, wasting/emaciation and cachexia are described as separate entities, although in clinical practice these forms of undernutrition co-exist and often cannot be distinguished from each other. A good example are the chronically ill elderly. Their nutritional status can deteriorate quickly by the disease related cachexia and a superimposed diminished nutritional intake by for example a general feeling of discomfort or reduced mobility. This makes taking care of one’s own meals difficult or even impossible, not even to mention the effect of life events, such as widowhood. These situations are unfavourable, next to the already physiologically reduced appetite in the elderly.³⁴ Especially when keeping in mind that even a balanced eating pattern of less than 1,500 Kcal (6.3 MJ) does not supply sufficient micro- or macronutrients (energy).³⁵

In a Dutch cross-sectional multi-centre study, the prevalence of undernutrition was 24% in hospitals, 22% in home care organizations and 19% in nursing homes according to (1) BMI ($<18.5 \text{ kg/m}^2$), unintentional weight loss (6 kg in six months or 3 kg in one month), or (2) BMI between 18.5 and 20 kg/m^2 in combination with no nutritional intake for three days or reduced intake for ten days.³⁶ In primary care, the prevalence of undernutrition is yet unclear and its exploration is one of the main goals of this thesis. We expect it to be high, since general practitioners interact between community, hospital and nursing home. According to Statistics Netherlands, 1.7% of the general Dutch adult

population had a BMI < 18.5 kg/m² between 2004 and 2007.³⁷

Daily practice and guidelines

Nowadays, undernutrition is often noticed in late stages by physicians and thought to be inevitable, especially when disease related. In fact, in case of an elderly patient, weight loss can be irreversible, since with ageing the normal mechanisms for conserving energy during periods of reduced food intake have been reported to fail.³⁸ Therefore, regular body weight measurement in patients at risk of undernutrition is attractive, as it opens the possibility of early appropriate treatment.

At this moment, the Dutch College of General Practitioners is preparing a national agreement (Landelijke Eerstelijns Samenwerkings Afspraak) on the collaboration of primary care workers (dietitians and district nurses) to enhance awareness and early intervention in case of undernutrition. Table 2 shows which guidelines of the Dutch College of General Practitioners should mention or already contain aspects of nutritional deficiency.

Table 2 Guidelines of the Dutch College of General Practitioners which are in some way related to nutrition deficiency or weight gain (overweight/obesity)

Nutritional deficiency	Weight gain (overweight/obesity)
<i>COPD</i>	<i>COPD</i>
<i>Cardio vascular accident</i>	<i>Cardio vascular accident</i>
<i>Depression</i>	<i>Depression</i>
<i>Diabetes mellitus type 2</i>	<i>Diabetes mellitus type 2</i>
<i>Heart failure</i>	<i>Heart failure</i>
<i>Hypo- and hyperthyroidism</i>	<i>Hypo- and hyperthyroidism</i>
<i>Rheumatoid arthritis</i>	<i>Rheumatoid arthritis</i>
<i>Subfertility</i>	<i>Subfertility</i>
Acute diarrhoea	Atrial fibrillation
Amenorrhoea	Cardiovascular risk management
Anaemia	Management after myocardial infarction
Delirium in the elderly	Peptic diseases
Dementia	Peripheral arterial disease
Irritable bowel syndrome	Smoking cessation
Osteoporosis	Transient ischemic attack
Pelvic inflammatory disease	Varicose veins
Pressure sores	Venous leg ulcer
Problematic use of alcohol	Viral hepatitis and other liver diseases
Venous leg ulcer	

In italics: guidelines related to both nutritional deficiency and weight gain (overweight/obesity).

Overweight/obesity

Overweight and obesity are the result of excess dietary energy compared to body expenditure. According to the WHO, obesity is a condition of abnormal or excessive fat accumulation in adipose tissue to the extent that health may be impaired. Obesity is a chronic disease, which acquires preventive measures, early case finding and lifelong treatment.³⁹

Consequences

The excessive weight of fat tissue on its own may contribute to clinical disorders. However, in addition to the weight of this energy substrate depot, fat tissue functions as a metabolically and immune active organ, which increases the atherogenic risk. Individual susceptibility depends on

how the fat is stored (adipogenesis), where it is stored (visceral versus subcutaneous) and upon the signalling and interactions with other body organs.⁴⁰

Obesity is related to (chronic) disorders or diseases, such as hypertension, diabetes mellitus type 2, hyperlipidemia and heart diseases, but also to subfertility, asthma, sleep apnoea syndrome, osteoarthritis, gallstones, gastroesophageal reflux disease, atrial fibrillation and certain types of cancer. Obese women more often have varicose veins and haemorrhoids.⁴¹⁻⁴⁸ Overall, obesity strongly decreases life expectancy.^{49;50} Mentally, overweight and obesity reduces self-esteem and in social aspects people are stigmatized, bullied or even discriminated against. Healthy overweight subjects have an increased extracellular fluid volume after a high sodium intake compared to their normal weight counterparts. Although no hypertension occurred, this might be an early pathogenic factor in the cardiorenal complications.⁵¹ In health care settings, a lower subjective health status and health-related quality-of-life have been reported in overweight and obese patients.^{52;53} The (health) related expenses of obesity are substantial: for the UK, for example, this has been estimated to be about 3.5 billion pounds per year.⁵⁴ In the Netherlands there has not yet been a study of the expenses of obesity.

In the development of effective treatment strategies to combat an excess weight on the long run, progression is being made.^{55;56}

Clinical assessment tools

The BMI is a widely accepted tool to classify overweight and obesity (table 1). Besides the BMI, the waist circumference is an additional reliable tool to establish the cardiovascular disease or even the overall mortality risk. Since the mortality risk is higher in those with a low-normal BMI and a high waist circumference.⁵⁷ The cardiovascular risk is increased in men with a waist circumference ≥ 102 cm and in women ≥ 88 cm.⁴⁸

Clinical and epidemiological aspects

From an evolutionary point of view, the human body has been built to store or maintain body fat.⁵⁸ This genetic predisposition in the nowadays obesogenic environment, causes a global growth of overweight and obesity. Patients at risk of becoming overweight or eventually obese, are those of a low social economical status, of non-European origin, in psychological distress or who have quit smoking.⁵⁹

In the Netherlands, according to self-reported data from 2007, 34% of the adults were overweight and 11% obese. These figures have tended to stabilize since 2000.⁶⁰ Unfortunately in children this is not the case, prevalence rates of overweight and obesity increased rapidly from 6% in 1980 to 15% in 2002-2004.⁶¹ Similar trends are seen in other European countries. By 2010, one-fifth of Europe's population will be obese.

Daily practice and guidelines

General practitioners predominantly provide weight management in adult patients with a high cardiovascular risk,⁶² although – as described earlier – more obesity related disorders or diseases exist.

Currently, the Dutch College of General Practitioners is developing a guideline on obesity. In table 2 the guidelines of the Dutch College of General Practitioners related to weight gain or an excess in body weight are displayed.

Outline of this thesis

Good nutrition is especially important in preventing diseases, but is also supportive in various treatments in general practice. Since in the near future the prevalence of nutritional deficiency – by an increased number of fragile elderly – and overweight/obesity will rise, general practitioners will more frequently face their health consequences.

The prevention of undernutrition is feasible if it is a prevalent phenomenon and has generally accepted clinical assessment tool(s) and treatment available, as is more the case in obesity. If undernutrition is rare in the adult general practice population, patient groups ‘at risk’ or/and predisposing factors need to be further explored. But above all, prevention starts with the awareness of general practitioners.

In part one of this thesis the main aim was to explore the frequency of nutritional deficiency/undernutrition, in the adult general practice population, and in specific ‘at risk’ groups. We summarized the clinical assessment tools used and applied those acceptable for general practice. Also, we were able to get more insight into the current management of undernutrition by general practitioners.

Chapter 2 is a systematic review, in which we reported the prevalence of nutritional deficiency and clinical assessments used in general practice studies. Chapter 3 displays the incidence and prevalence rates of nutritional deficiency extracted from Dutch general practice research and registration networks. In chapter 4 and chapter 5, the prevalence of undernutrition is described in a cohort of head and neck cancer patients and a cross-sectional study in COPD patients, respectively. In the study concerning head and neck cancer patients, we also surveyed nutrition related documentation in referral letters and medical records by general practitioners. As there is shortage of empirical data of undernutrition in general practice, we described and analyzed the medical history of two patients in depth. This is published in the format of a case report in paragraph 4.1. In chapter 5 we established the association of nutritional depletion with COPD severity and aging, as well as predisposing factors. This knowledge can help to target care for those at the highest risk.

Obesity is described in literature in much more detail than undernutrition, still much is unknown of its effect on – or relation with – other morbidity. The second part of this thesis was dedicated to link obesity to health related consequences in general practice from a single chronic disease (COPD) to multiple common illnesses and the implications for daily practice.

We compared the frequency of encounter for episodes of the ten most common illnesses in general practice between obese and non-overweight patients in chapter 6. This is backed-up by two further explorations. Paragraph 5.1 comprises a letter to the editor, which illustrates the effect of obesity on lung function and experienced dyspnoea in COPD patients. And in paragraph 6.1, we explored the community oriented role of the general practitioner, based on our findings in the obesity epidemic (letter to the editor).

The thesis is reflected upon, in chapter 7, which discusses the main conclusions of the studies. This chapter closes with a broad, partly consensus based, scope on the general practitioners’ proposed role in malnutrition against the background of current and future developments in the field of nutrition.



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PART ONE ||| CHAPTER 2

Nutritional deficiency in general practice: a systematic review

European Journal of Clinical Nutrition (2005) 59, Suppl 1, S81–7; discussion S88

Abstract

Objective: Nutritional deficiency is an independent risk factor for mortality. Despite its clinical relevance, the prevalence in a primary care setting is poorly documented. We performed a systematic review of reported prevalence and clinical assessment of nutritional deficiency in general practice.

Methods: From MEDLINE, Current Contents and EMBASE, we derived articles and checked the initially included ones for references on prevalence data. Of the eligible articles, we assessed the quality of research and results.

Results: We finally included eight studies. The prevalence ranged from 0 to 13%. However, the study populations were heterogeneous and all studies contained methodological flaws, especially selection bias. In addition, the clinical assessment differed between studies.

Conclusion: Literature on the prevalence of nutritional deficiency within general practice is rare and provides disputable prevalence assessments.

Introduction

In modern Western society, an unbalanced eating pattern has far reaching health consequences.⁶³ Obesity, a result of excess dietary energy compared to body expenditure, is well documented and highly prevalent. This is in contrast to nutritional deficiency, which seems to be virtually unrecorded. However, particularly in the chronically ill elderly, the risk of developing nutritional deficiency is substantial.³³

Unlike the term malnutrition, which implies a wide range of nutritional disorders, including deficiency or excess (or imbalance) of energy, protein and other nutrients,⁶⁴ nutritional deficiency specifies undernutrition in early as well as advanced stages.

Implications of nutritional deficiency vary from delayed wound healing,^{14;65} and deterioration of muscle function^{66;67} to impaired immune function.¹⁵ Undernourished patients show a higher consultation and prescription rate,¹⁸ longer hospital stays,²² a reduced quality of life²³⁻²⁵ and most importantly an increased mortality risk.^{16;17;19;20;68;69} Yet, the prevalence of nutritional deficiency within primary care has not been systematically reviewed.

Particularly, the elderly are less capable of recovering from weight loss.^{70;71} Therefore, nutritional deficiency should be treated in its early stages. Universal prevention belongs partly and selective prevention completely to the domain of primary health care. Furthermore, the general practitioner faces an increasing population 'at risk' for nutritional deficiency. The European population is aging, as a result of a fertility fall and longevity rise. Between 1995 and 2015, the population aged over 65 years is expected to grow by 30%, for the very old (80+), this will be 40%, as a consequence morbidity will rise.⁷² For family practice, the effect of this will be re-enforced by the trend of home care, instead of hospitalisation.

We performed a systematic review to obtain a literature overview of the prevalence and clinical assessments of 'nutritional deficiency' in general practice.

Methods

Inclusion criteria were cohort, cross-sectional or nutrition surveys concerning prevalence of nutritional deficiency. The subjects studied had to be adults (≥ 18 years), living in developed countries (North America, Europe, New Zealand and Australia) and recruited from primary health care. We included study populations 'at risk' for nutritional deficiency and all languages of publication. We excluded studies concerning eating disorders as well as studies of which no full report was available (e.g. abstract or poster).

We developed a sensitive search strategy that combined (key) words for general practice and synonyms, nutritional deficiency and synonyms and study-type and epidemiological variables (prevalence or incidence) (table 3).

In June 2003, we searched MEDLINE (1966-2003), Current Contents (1996-2003) and EMBASE (1980 Week 25-2003). Two independent reviewers (CvWa, FvdL) read all titles and/or abstracts and scored them for eligibility by inclusion and exclusion criteria listed (figure 2). In case of doubt, we read the full contents of the article. We calculated the inter-reviewer agreement in article selection by kappa statistics. One reviewer (CvWa) checked initially included articles for references on prevalence values. And both reviewers (CvWa, FvdL) assessed possible suitable references and extracted data from all finally included articles by use of a pretested data-extraction matrix.

Table 3 Synonyms in search strategy

Setting	General practice/practitioner Primary (health) care Family practice/doctor/physician/medicine Other: outpatient care or primary medical care or private practice
Variable	(Adolescent/under) nutrition (assessment/disorders) Weight loss/reduction Emaciation Cachexia Kwashiorkor Marasmus Wasting syndrome (Protein (calorie/energy)) malnutrition Sarcopenia Underweight Low (/lean) body mass Lean body weight Undernourish Thinness Nutritional support/status/requirement Diet therapy Dietary intake Muscle atrophy Other: diet/or feeding behaviour/or food/or food intake/or meal/or nutrient/or nutritional tolerance
Study type and epidemiological variables	Cross-sectional study Prevalence, incidence Epidemiology Cohort (analyses/-studies) Nutrition survey

We determined the quality by the internal and external validity. The internal validity refers to the degree of certainty that the observed results are truthful, and depends on the study methodology. We evaluated selection bias (selection methods and/or non-response bias) and information bias (abstracted data from medical files, interview bias, recall bias and reporting bias). The external validity is the extent to which we can extrapolate the results to the general population. It comprised gender and age distribution of the study population, country, study design, objective, inclusion and exclusion criteria, number of patients and of general practitioners participating.

We compared the studies on basis of the clinical assessment of nutritional deficiency and external validity.

Results

Figure 2 shows the inclusion and exclusion pathways of articles. Searches in MEDLINE, Current Contents Archives/Weekly and EMBASE yielded 577, 436 and 871 records, respectively. Most articles dealt with obesity and its health effects and were excluded. Initially, we included 24 articles by title and abstract. After further analysis, we excluded 17 articles. The inter-reviewer kappa was 0.68 (95% confidence interval (CI) 0.54-0.83). From the references of the initially included articles, we included one additional study.⁷³ Articles were excluded because they did not describe prevalence studies (e.g. narrative reviews) or did not concern a general practice population (e.g. community dwelling).

Figure 2 Article selection pathway

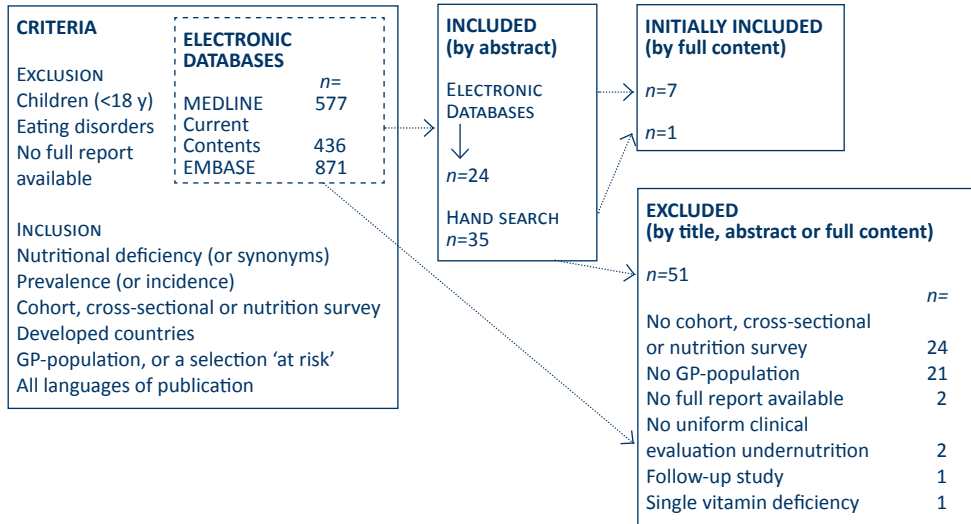


Table 4 gives an overview of the internal and partly the external validity of the articles included. Within studies, the percentage of males differed from 25 to 100%. The mean age was above 55 years. Description of selection methods in all studies missed important aspects with regard to the study population and/or the general practice characteristics. Furthermore, the participant rate, the number, characteristics and reasons of non-participants were not described. Information bias was mainly caused by self-reported data on height and weight or unclear definitions of undernutrition.

Table 5 gives an overview of the external validity and results. Four studies were conducted in the United Kingdom (UK), the others in Denmark, the United States of America (USA) and the Netherlands. Six studies were cross-sectional and two were retrospective. Most articles failed to describe the exclusion criteria, as well as the number of general practitioners participating. The prevalence of nutritional deficiency ranged from 0 to 13% depending on the study population and clinical assessments. Only two studies^{74;75} presented a prevalence with CI. There was a large variation in recruitment methods (patients visiting the general practitioner or contacted for research participation), in mean age of the study population and in the presence of co-morbidity.

We divided study populations into three groups: (1) ill patients (cancer, chronically ill, post-surgery), (2) elderly population (≥ 65 years), and (3) a general population. Four studies concerned the ill patients, three the elderly and one the general population.

We classified three categories of clinical assessments of nutritional deficiency: (1) The Body Mass Index (BMI), with/or without Triceps Skin-Fold thickness (TSF) or Mid-arm Muscle Circumference (MMC), (2) presence of weight loss in time and (3) the Mini Nutritional Assessment (MNA). The BMI was calculated by body weight divided by height² (kg/m²) and the MMC by mid-arm circumference (cm) x 0.314 TSF (mm). TSF was measured with skin fold callipers. The MNA is a questionnaire of four categories (a total of 18 questions), concerning anthropometric measurements (e.g. weight loss), a global assessment (e.g. questions related to lifestyle), dietary questions (e.g. number of meals) and a subjective assessment (e.g. self-perception of health). The calculated score

Table 4 Internal validity and external validity (gender distribution, mean age and number of GP participating)

Study	Male (%)	Mean age (y)	Selection methods	Selection bias	Information bias
Ill patients					
Edington <i>et al</i> (1996)	58	68 (range 22-93)	25 GPs with computerised records Included a random sample of patients, stratified by gender and practice Patients actively contacted; participant rate: 80% Reasons of non-participation described	Selection method of GPs not specified Stratification only for the first 20 practices Non-participants not described by age and gender	Random
Edington <i>et al</i> (1997)	60	64 (range 23-90)	24 GPs with computerised records Registered patients included Patients actively contacted; participant rate unknown	Selection method of GPs not specified No stratification, no random sample Non-participants not specified by number, reason of refusal, age and gender	Random
Kruizenga <i>et al</i> (2003)	Unknown	64.5 (range 18-102)	91 teams of dieticians in different fields (GP: $n=22$ locations) Patient selection not specified Participant rate unknown	Selection method of dieticians not specified Non-participants not specified by number, reason of refusal, age and gender 923 patients excluded because of incomplete data	Height self-reported or measured (not described)? Unintentional weight loss was asked Supplementary information (e.g. kind of illness) obtained from medical records Number of participants in primary and home care not equal between tables Prevalence of undernutrition in primary and home care not equal between table and text
Martyn <i>et al</i> (1998)	45	55.7 (range 18-96)	General Practice Research Database (>500 practices) Included registered patients who visited the GP	No stratification, no random sample Selection of people whose weight and height was previously measured	Random
Elderly population (with(-out) co-morbidity)					
Beck <i>et al</i> (2001)	30	75 (95% CI 72-79)	Patients included at GP consultation Participant rate: 65% Non-participants and participants similar in age and gender	Selection method and number of GPs not specified	Height and weight self-reported in 98% of the participants MNA: neuropsychological problems based on subjective impression

Study	Male (%)	Mean age (y)	Selection methods	Selection bias	Information bias
Elderly population (with(-out) co-morbidity)					
DeVore (1993)	25	78	One GP included visiting patients, inclusion criteria unclear Participant rate: 100%	Informed consent is not mentioned	Weight and height self-reported or measured (not described)? Definition of underweight unclear
Wissing <i>et al</i> (1999)	28	79 ($\pm$ 6.5)	Nine primary care areas Nurses identified included patients; participant rate: 64% Non-participants and participants did not differ in age and gender Reasons of non-participation described	Selection methods of participants with ulcers unclear Inclusion by nurses is doubtful reproducible Patients under care of a specialist were also included	Height and weight measured (except two patients who could not stand. Of them self-reported data were collected of last hospital stay or clinic visit)
General population					
Wannamethee <i>et al</i> (2000)	100	67 (range 57-78)	24 general practices in different towns Included random sample of patients, stratified by town and age, selected from a age-gender register Patients actively contacted: participant rate: 78%	Towns were selected by regional variation in cardiovascular disease and water quality Included patients had to report weight information in two subsequently questionnaires	Definition of weight loss not further specified Body weight self-reported

Table 5 External validity and results

Study	Design	Objective	Inclusion	Exclusion	Subjects (n)	Clinical assessment of nutritional deficiency	Results
Ill patients							
Edington <i>et al</i> (1996), UK	Cross-sectional	Prevalence of undernutrition, etc.	≥18 y, co-morbidity ^a	Not described	441	Deficient: BMI<20 and TSF or MMC<P15	9% (CI 6.3-11.8%) Cancer: 10% (CI 6.2-14.5%) Chronic disorder: 8% (CI 4.3-11.5%)
Edington <i>et al</i> (1997), UK	Cross-sectional	Prevalence of undernutrition	>18 y, surgery ^b within 6 weeks	Not described	123	See Edington <i>et al</i> (1996)	(1) 10.6% (CI 5.0-16.1%)
Kruizenga <i>et al</i> (2003), the Netherlands	Cross-sectional GP (7%, n=533 or 558?) H (81%), I (11%), U (1%)	Prevalence of disease related undernutrition	Not described	<18 y, patients who could not be weighed	7,606	Unwanted weight loss during the last 6 months: (1) Deficient: >10% (2) At risk: 5-10%	Population of a GP: (1) 5 or 6%? (n=31) (2) 7% (n=40)
Martyn <i>et al</i> (1998), UK	Retrospective cohort Follow-up: 2.4 y, sd 1.5 y	Relation use health care resources and nutritional state	>18 y with diagnosis of chronic disease ^c	BMI<15 and BMI<40 in further analyses	11,494	(1) BMI<15 (2) 15≤BMI<20	(1) 0.4% (2) 12.1%
Elderly population (with-out) co-morbidity)							
Beck <i>et al</i> (2001), Denmark	Cross-sectional	Frequency nutritional risk, etc.	>65 y, not acutely ill	Not described	61	(1) Deficient: MNA<17 (2) At risk: 17≤MNA≤23.5	(1) 0% (2) 38%
DeVore (1993), USA	Cross-sectional	Prevalence of overweight/obesity, etc.	≥65 y	None	122	(1) Underweight BMI (cutoff point unclear)	(1) 11.6% Men: 16.7% Women: 6.5%
Wissing <i>et al</i> (1999), Sweden	Cross-sectional	Nutritional status in patients with leg and foot ulcers, etc.	≥65 y, own home, treated for leg and foot ulcers ^d , contacted for participation	Not described	70	(1) Deficient: MNA<17 (2) At risk: 17≤MNA≤23.5	(1) 3% (2) 46%
General population							
Wannamethee <i>et al</i> (2000), UK	Retrospective and prospective cohort Follow-up: Not described	Characteristics and health status of men who lost weight with aging	Men, aged 40-59 y, contacted for participation	Severe mental or physical disability	4,534	(1) Weight loss Intentional Unintentional	(1) 18% 7% 11%

Supplementary information is available at <http://www.nature.com/jecln/>. ^a Cancer of the lung, prostate, or gastrointestinal tract, and chronic diseases of the lung, gastrointestinal tract, or neurological system. ^b Orthopaedic, cardio-thoracic, gastrointestinal or genito-urinary. ^c Respiratory, gastrointestinal and neurological disease, including Chronic Obstructive Pulmonary Disease (COPD), chronic bronchitis, emphysema and bronchiectasis, cirrhotic liver disease, chronic liver disease, chronic hepatitis, Crohn's disease, ulcerative colitis, chronic pancreatitis and chronic intestinal malabsorption, Parkinson's disease and recorded since January 1988. ^d Foot ulcers open for more than one month, not expected to heal within six weeks.

CI=Confidence Interval; sd=standard deviation; FL=free living; GP=general practitioner; H=hospital; I=institution; MNA=Mini Nutritional Assessment; U=unknown; MMC=Mid-arm Muscle Circumference; TSF=Triceps Skin Fold thickness.

estimates the (risk of) nutritional deficiency.

In four studies, the BMI, with or without TSF or MMC was used as clinical assessment for nutritional deficiency. The largest study¹⁸ found a prevalence of 13% of nutritional deficiency in chronically ill patients. Another study⁷⁴ reported prevalences of 8% and 10% in chronically ill and cancer patients, respectively. They combined BMI with TSF or MMC. The same clinical assessment method was applied in patients after major surgery, resulting in a prevalence of 11%.⁶¹ One study did not specify the cutoff point of BMI for classifying nutritional deficiency but reported a percentage of 12%.⁷⁶

In two studies,^{32;77} weight loss was used to assess the nutritional status. Wannamethee *et al* reported unintentional weight loss in 11% of males, but unintentional weight loss was not predefined quantitatively.⁷⁷ The other study³² defined undernutrition as weight loss more than 10% in six months and 'at risk' between 5-10% weight loss. The study was conducted from a dieticians' point of view with patients from several health settings. The general practitioner referred 7% of the patients included, of which a total of 5 or 6% (data not equal in text and table) were undernourished.

Two studies assessed the risk of nutritional deficiency with the MNA; however the study populations differed. One concerned not acutely ill elderly visiting their general practitioner,⁷⁸ the other reported elderly with foot ulcers contacted for research purposes.⁷³ The prevalence of undernutrition was 0 and 3%, respectively.

Discussion

Literature on the prevalence of nutritional deficiency in general practice is rare and gives a disputable prevalence assessment. The prevalence ranged from 0 to 13%. Owing to failure to adjust for possible confounders (e.g. gender-, age- and nutrition-related illnesses) within studies, reported prevalence must be interpreted as crude. The overall quality of the included articles was poor, with selection bias the weakest link. Edington *et al* stratified for gender and general practice to compare the chronically ill and cancer patients.⁷⁴ Kruijenga *et al* reported data concerning patients referred to a dietician.³² Hence, these results cannot be interpreted as the prevalence of disease related undernutrition in primary care setting.

This reported prevalence of nutritional deficiency in primary care is low, compared to nursing homes, 10-40%⁷⁹ and hospitals, 20-62%.^{22;80;81} The general practitioner refers patients for more diagnostics or intensive treatment or care to these care settings daily. This selection partly explains the difference in prevalence of nutritional deficiency between hospital and primary care.

Although patients in hospital have been studied more systematically, these studies suffer from the same methodological problems. McWhirter *et al* and Edington *et al* assessed prevalence of nutritional deficiency on admission, based on BMI and TSF or MMC,^{80;81} which were 40 and 20%, respectively. Naber *et al* on the other hand, reported a prevalence of 45, 57 and 62%, according to the Subjective Global Assessment (physical examination and questionnaire), the Nutritional Index (e.g. calculation formula with blood levels) and the Maastricht Index (e.g. calculation formula with blood levels), respectively, on admission of (gastro) intestinal patients.²² The study of Edington *et al* illustrates the importance of reporting non-participation in estimating nutritional deficiency, because nearly half of the patients refused or could not participate. They were too ill and it is likely that many of them suffered from nutritional deficiency.

Studies in the open population show a prevalence of 0 to 34% with the same clinical evaluations as mentioned in table 5.⁸²⁻⁸⁶ This is more in line with our findings and suggests that the population registered in general practice is comparable to the community.

There is no universal agreement on the definition and clinical assessment of nutritional deficiency and this hampers comparison of studies. This reflects the complexity of the genesis of nutritional deficiency. From a medical point of view, nutritional deficiency results from loss (e.g. vomiting), decreased food intake/tissue storage (e.g. protein)/intrinsic production (e.g. vitamin D), and/or increased demand. Despite these different aetiologies, they all cause measurable adverse effect on body shape/composition/function, and have a negative influence on clinical outcome. For example, an energy intake below 1,500 kcal (6.3 MJ) can serve as a definition of inadequate in the elderly,³⁵ eventually resulting in weight loss. A daily intake of less than 1,500 kcal is not only insufficient of macro- but as well as some micronutrients.

The methods for this review were adapted from Cochrane guidelines.⁸⁷ However, in contrast to Cochrane reviews, this review concerned prevalence studies instead of randomised clinical trials or controlled clinical trials. Still we aimed to apply similar rigorous methods to minimise observation and selection bias.

We conclude that better quality data on nutritional deficiency, and a clear definition is needed. In order to understand the impact in primary care better. Data must be presented in different gender, age and/or illness categories to establish an accurate prevalence and to identify 'at risk' populations.

Acknowledgements

We thank the Dutch Dairy Association for the financial support, Rob Scholten for the EMBASE contribution and Caroline Roos for translating the Spanish articles.



Caroline A.M. van Wayenburg
Floris A. van de Laar
Margot W.M. de Waal
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PART ONE ||| CHAPTER 3

Nutritional deficiency in Dutch primary care: data from general practice research and registration networks

European Journal of Clinical Nutrition (2005) 59, Suppl 1, S187–94

Abstract

Objective: To explore incidence and prevalence rates of nutritional deficiency in adults in general practice.

Methods: Six Dutch general practice research and registration networks supplied incidence and prevalence rates of nutritional deficiency by the International Classification of Primary Care (ICPC) or 'E-list' labels ('loss of appetite, feeding problem adult, iron, pernicious/folate deficiency anaemia, vitamin deficiencies and other nutritional disorders, weight loss'). In case of disease related nutritional deficiency, we asked whether this was labelled separately ('co-registered') or included in the registration of the underlying disease.

Results: 'Iron deficiency anaemia' had highest incidence (0.3-8.5/1,000 person years), and prevalence rates (2.8-8.9/1,000 person years). Nutritional deficiency was mostly documented in the elderly. In two networks 'co-registration' was additional, two only documented the underlying disease and two did not specify 'co-registration'. No clear difference was found between networks considering the difference in 'co-registration'.

Conclusion: Nutritional deficiency is little documented in general practice, and generally is not registered separately from the underlying disease.

Introduction

Nutritional deficiency is a state of insufficient intake (e.g. loss of appetite, nausea), absorption (e.g. diarrhoea, decreased intrinsic factor), utilization (e.g. inflammation), tissue storage (e.g. protein), intrinsic production (e.g. vitamin D) and/or increased loss (e.g. vomiting, burns, menstruation) over time. Nutritional deficiency can be a micronutrient deficiency (e.g. iron, vitamins), and in advanced stages accompanied by macronutrient deficiencies (protein-energy undernutrition). Advanced nutritional deficiency can be quantified by muscle mass depletion or weight loss. It negatively influences quality of life,²³⁻²⁵ and above all increases the risk of mortality.^{16;17;19;20;68;69}

Cancer and chronic diseases, such as Chronic Obstructive Pulmonary Disease (COPD) and heart failure, are frequently accompanied by advanced nutritional deficiency, caused by a hyper-metabolic state, which may be aggravated by a reduced appetite, also referred to as cachexia.^{4;7}

Anorexia of aging is an often described syndrome in the elderly, and together with a sedentary life style it may lead to muscle depletion, called sarcopenia.³⁴ For this reason elderly people, particularly when suffering from chronic diseases, are at increased risk for nutritional deficiency. We previously found in the literature, the prevalence rates for nutritional deficiency in general practice of 9-13% (chronically ill) and 0-12% (elderly).⁸⁸ However, only few studies were available and all had methodological flaws.

General practice research and registration networks (further referred to as 'networks') might be a source of data on prevalence and incidence. In the Dutch health care structure patients are listed with one general practice (group), which provides their personal professional medical care, including referrals to medical specialists.⁸⁹ Therefore, networks can establish a precise denominator for incidence and prevalence calculations. Currently, more than 80% of the general practitioners (GPs) use an electronic medical patient record in their daily practice.⁹⁰ Conclusively, this is an excellent resource for networks.

The aim of this study was to explore incidence and prevalence rates of nutritional deficiency in adults (15 years and older) in Dutch general practice.

Methods

In October 2003, we sent a letter of invitation to the management of all 14 networks;⁹¹ subsequently, we contacted them by telephone. Three networks had ceased to exist, two were unable to cover administration fees required to supply data, two networks were unable to provide the diagnostic labels required for this study, and one was declined for pragmatic reasons. Six networks were therefore included.

The classifications used in the participating networks, the International Classification of Primary Care (ICPC) or the 'E-list', are based on equal diagnostic criteria of the International Classification of Health Problems for Primary Care (ICHPPC).⁹² From these classifications⁹³ we compiled a list of nutrition deficiency-related symptoms and diagnoses: 'Loss of appetite, feeding problem adult, iron deficiency anaemia, pernicious/folate deficiency anaemia, vitamin deficiencies and other nutritional disorders, and weight loss'.

We requested incidence and prevalence rates (total, and subdivided into gender and preset age groups) of the corresponding labels. The incidence rate was defined as the number of (patients

with ≥ 1) 'new' recorded episode(s) (or problem(s)) per 1,000 patient years (at risk). The prevalence rate was defined as the number of (patients with ≥ 1) 'new' or 'still clinically relevant' episodes (or problems) per 1,000 patient years (at risk). An episode is the period from the first presentation of the disease or health problem at the GP until the last contact.

Additionally we asked if, in case of disease related nutritional deficiency (e.g. weight loss in patients with cancer), this was labelled separately ('co-registered') or included in the registration of the underlying disease.

In the Transition project and the 2nd National Study (NS2) 'co-registration' was additional. The Continuous Morbidity Registration (CMR) and the Registration Network Family Practices in Maastricht (RNH) document only the underlying diagnosis (at the highest level of certainty), and the Registration Network Groningen (RNG) and the Registration Network University Family Practices, Leiden and its environs (RNUH-LEO) did not specify 'co-registration'.

Summary of the basic background of participating networks

1. *Transition project*,^{94;95} from 1985 to 1995, comprised 23 general practice(s) (groups) with 54 GPs in Amsterdam and the north of the Netherlands. Each GP collected data during a period of at least one year. The mean registration period was 2.4 years. Participating GPs order and label each encounter, the patient's reason for the encounter, the diagnoses, and the interventions. A diagnosis can be modified during the course of an episode.
2. *NS2*^{96;97} took place during May 2000-April 2002 in 104 general practice(s) (groups) with 195 GPs. The prevalence and incidence calculations are based on 96 practices all over the Netherlands. The study is a representative sample of Dutch GPs and their practice population (e.g. in age, gender, geographic distribution, urbanization, pharmacy containing practices). Recording of a recurring 'new' episode was only allowed after an interval of 28 days or more.
3. *CMR*⁹⁸⁻¹⁰⁰ started in 1971 and contains data collected by four general practice(s) (groups) with 10 GPs in Nijmegen and surroundings. From the start, a diagnosis is labelled according to the 'E-list'^{101;102} to guarantee tracking of morbidity over time ('longitudinal research').
4. *RNH*¹⁰³ was set up in 1988 and holds 22 general practice(s) (groups) with 65 GPs in the South of the Netherlands. They register on-going (no recovery expected), chronic (duration longer than six months), and recurrent health problems (more than three recurrences within a period of six months) and problems with a high impact on daily functioning. Self-limiting minor illnesses are not registered.
5. *RNG*^{104;105} was established in 1989 and includes 6 general practice(s) (groups) with on average 15 GPs in the north of the Netherlands.
6. *RNUH-LEO*¹⁰⁶ started in 1989 and contains four general practice(s) (groups) with in total 20 GPs.

Differences in participating networks

- The scientific mission; The Transition project and CMR are specifically grounded for research, and the NS2, RNH, RNG, RNUH-LEO provide a sampling frame by optimized standard electronic patient records.
- Agreement in coding morbidity within networks; the Transition project, NS2 and RNUH-LEO apply merely ICCPC-criteria,⁹² whereas the CMR, RNG and RNH supply feedback by (regular) meetings.
- All networks register episodes except the RNH, which documents chronic/recurrent episodes as problems.

- The registration of diverse patient-GP contacts, such as ‘face to face’ patient contacts (home and office visits) (all networks), telephone consultation (all, except the RNG), contact with the assistant (all, except the RNH and RNG), referrals (e.g. to the hospital) (all, except the RNH), diagnoses from the patient’s contact with the specialist without the interference of the GP (e.g. first aid) (only the CMR), medication prescription resulting in episode labelling (all, except the CMR and RNH) and out of hours (e.g. shifts, holidays) (all networks).

Analyses

In the Transition project labels can be classified as ‘certain’ or ‘uncertain’. Some presented labels are symptoms and for this reason relatively ‘uncertain’ – not objective or not totally matching the label inclusion criteria – therefore we analysed ‘uncertain’ as well as ‘certain’ labels. Additionally, we present the reason for encounter, only available for the Transition project, during the first contact with the GP (at start) and the reason for encounter during all contacts (total) expressed per 1,000 patient years (at risk).

The presented rates for those aged 15 years and older were directly standardized for the Dutch population during the observation years.

Results

Figure 3 shows the distribution of the GPs from the included networks in the Netherlands. Table 6 summarizes population characteristics of each network. The overall population, in terms of age and gender distribution, of the six networks was comparable to the Dutch population, with a slight over-representation of adults aged 25-44 years (table 6) and women. The population of the Transition project contained the highest proportion of elderly, the majority of them women.

Figure 3 Distribution of the GPs participating in six networks in the Netherlands



Table 6 Characteristics of the populations (in patient years/year) of Dutch general practice networks, and the difference (%) between the gender and preset age groups with the total Dutch population during the observation period (network% - Statistics Netherlands%) (<http://www.cbs.nl/nl-NL/menu/themas/bevolking/cijfers/extra/piramide-fx.htm>)

		Transition project ^a	NS2 ^b	CMR	RNH	RNG	RNUH-LEO
Patient years	All ages	38,874	375,899	13,310	97,935	29,050	28,153
	15-24	5,043 (-3.7)	46,549 (0.6)	1,262 (-2.9)	11,284 (-0.8)	3,591 (-0.1)	3,641 (1.2)
	25-44	12,565 (-1.1)	121,241 (1.3)	4,456 (3.6)	30,384 (-1.2)	10,339 (3.9)	9,399 (2.8)
	45-64	7,434 (-3.2)	91,788 (-0.7)	3,337 (0.3)	25,985 (1.1)	7,167 (-1.8)	7,319 (1.0)
	65-74	4,412 (4.4)	26,907 (-0.5)	981 (-0.1)	8,699 (1.4)	1,768 (-2.1)	1,576 (-2.4)
	75+	3,361 (3.6)	21,013 (-0.7)	710 (-0.9)	5,775 (-0.5)	1,883 (0.1)	1,174 (-2.5)
	15+	32,815 (0)	307,498 (0)	10,746 (0)	82,126 (0)	24,749 (0)	23,109 (0)
Gender	♂% (15+)	47.0 (-2.1)	49.3 (0.2)	49.1 (0.1)	48.4 (-0.7)	48.3 (-0.8)	49.6 (0.5)

^a Total patient years divided by the mean registration period (2.4 y).

^b The 'mid-time' population (based on the mean of the population at start and at the end of the study period concerning size, age, gender and insurance type).

CMR=Continuous Morbidity Registration; RNH=Registration Network Family Practices; RNG=Registration Network Groningen; RNUH-LEO=Registration Network University Family Practices, Leiden and its environs; NS2=2nd National Study.

Table 7 presents the incidences. 'Iron deficiency anaemia and weight loss' were the most documented incidence rates, 0.3-8.5 and 0.1-2.9 episodes/problems per 1,000 patient years, respectively. In decreasing order 'pernicious/folate deficiency anaemia, vitamin deficiency and other nutritional disorders, loss of appetite and feeding problem adult' have lower incidence rates, 0-1.9 episodes/problems per 1,000 patient years.

Table 8 presents the prevalences. The most prevalent, again, were 'iron deficiency anaemia and pernicious/folate deficiency anaemia', 2.8-8.9 and 1.5-6.2 episodes/problems per 1,000 patient years, respectively. These were followed by the prevalence of 'weight loss, vitamin deficiency and other nutritional disorders, loss of appetite and feeding problem adult', which varied from 0 to 3.2 episodes/problems per 1,000 patient years.

The period of care for the registered episodes/problems (difference between incidence and prevalence) was longest for 'pernicious/folate deficiency anaemia' and least for weight loss. In all labels, except for 'feeding problem adult', the incidence and prevalence rates were highest among elderly people aged over 75 years (incidence 0-24.1 per 1,000 patient years, prevalence 0-53.7/1,000 patient years). Also eye-catching was the high occurrence of 'iron deficiency anaemia' in fertile women. No clear difference in incidence and prevalence rates were identifiable between networks, considering the difference in 'co-registration'.

The reason for encounter rates (at start and total) were equal or higher than the incidence and prevalence rates for all nutritional deficiency related symptoms ('loss of appetite, feeding problem adult, and weight loss'), but lower for the related diseases: 'iron, pernicious/folate deficiency anaemia and vitamin deficiency and other nutritional disorders' (0.0-4.7 per 1,000 patient years). It becomes clear that patients, during follow-up of their episodes, present their reason for visit more often as a diagnosis ('iron and pernicious/folate deficiency anaemia').

Discussion

Iron deficiency anaemia and weight loss were the most reported incidence rates of nutritional deficiency (0.3-8.5 and 0.1-2.9 episodes/problems per 1,000 patient years, respectively). Patients present weight loss, a symptom as well as a diagnostic tool for advanced nutritional deficiency,

more often than the GP documents, as in secondary prevention. However, obesity and unintentional weight loss, of more than 10% in half a year,¹⁰⁷ might have a future in primary prevention.

The substantially lower incidence rate, as compared to prevalence rate, for ‘pernicious anaemia’, indicates that after the diagnosis it continues to be a clinically relevant problem as can be expected for a chronic disease. To a lesser degree this can be observed in iron deficiency anaemia and weight loss. The ‘short’ course can be explained by the fact that patients ‘recover’ quickly or die within a short period of time.

Comparison to the literature

The few empirical data on nutrition deficiency in primary care reported percentages of 0-13%,⁸⁸ which suggests a (much) higher impact of morbidity than came forward from the data of the networks presented. The elderly aged 75 years and older could be clearly identified as a population at risk for nutritional deficiency, which is in line with the literature.¹⁰⁸

Obesity, another nutritional disorder (not included here), seems to be a chronic condition, as indicated by the difference in incidence and prevalence in the CMR (2 and 42, respectively),² that is in contrast to nutrition deficiency in this study. Literature indicates a higher mortality risk for the undernourished patient^{16;17;19;20;68;69} and in particularly the elderly have a diminished capability to ‘recover’ from weight loss.^{70;71}

Methodological reflections

‘Weight loss’ can be interpreted as intentional (e.g. by a reducing diet) and unintentional (e.g. in cancer patients). Intentional weight loss is not an indicator for undernutrition and can therefore cause misclassification bias, although the ICCPC-criteria refer to weight loss/cachexia.

There are clear differences between the six networks with regard to their scientific mission, which would explain some variation in recording methods. Most obvious is the low recording rate in the RNH, especially for the incidence, explained by the limitation to record chronic/recurrent episodes.

Particularly important in this study was the question whether disease related nutritional deficiency was labelled separately (‘co-registered’) or included in the registration of the underlying disease. Surprisingly, we did not find higher prevalence and incidence rates in the Transition project and NS2, compared to the other networks. This might indicate that GPs register nutritional deficiency indirectly in the ‘causal’ (chronic) disease, and not separately, surprisingly also in the case of iron deficiency anaemia. This explains the lower reported prevalence expected from nutrition deficiency directed studies, besides methodological aspects (e.g. the retrospective nature of this study).

Considering the severe consequences; delayed wound healing,^{14;65} deterioration of muscle function,^{66;67} impaired immune function,¹⁵ longer hospital stays²² and a higher morbidity risk, it would be advisable to co-register nutritional deficiency to ensure optimal treatment and good management (e.g. in referral letters to the hospital).

Conclusion

The incidence of nutrition deficiency as found in networks seems to be low in general practice. However, it is in all probability only the tip of the iceberg of what GPs encounter. In contrast to obesity, GPs encounter nutrition deficiency in the context of other morbidity. There is a need for better insight, and on the basis of this review it is recommended to seek empirical data in an

indepth analysis of patients with chronic diseases or cancer in general practice.

Acknowledgment

We thank the Dutch Dairy Association for financial support, E.H. van de Lisdonk for the information on networks and H. Bor for 'statistical' support.

Table 7 Incidence (and reasons for encounter rate (at start)^a) (n/1,000 patient years) of registered nutritional deficiency related diagnoses for gender and preset age groups in Dutch general practice networks

ICPC/ E-list label (CMR)	Diagnosis	Age	Transition project ^{a,b} 1 Feb. 1985- 1 Jan. 1995		NS2 ^{b,c} 1 May 2000- 30 April 2002		CMR ^b 1 Jan. 1999- 31 Dec. 2003		RNH ^d 1 May 2000- 30 April 2002		RNG ^d 1 Jan. 1999- 31 Dec. 2003		RNUH-LEO ^b 1 Aug. 1998- 1 Aug. 2003	
			♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
T03 /2920	Loss of appetite /Anorexia ecl. anorexia nervosa	Years												
		15-24	0.7 (1.9)	1.1 (2.2)	0.1	0.5	0.0	0.0	0.0	0.1	0.0	0.4	0.2	0.3
		25-44	0.4 (0.6)	0.8 (1.6)	0.1	0.1	0.0	0.1	0.0	0.0	0.1	0.2	0.1	0.2
		45-64	0.4 (1.0)	0.3 (0.8)	0.1	0.1	0.0	0.0	0.0	0.0	0.1	0.2	0.1	0.1
		65-74	0.2 (1.5)	0.7 (2.2)	0.3	0.2	0.0	0.0	0.0	0.0	0.3	0.0	0.5	0.2
T05 /1061	Feeding problem adult /Nutritional disorders	75+	0.3 (2.0)	1.6 (4.7)	0.7	1.0	0.8	0.0	0.0	0.0	0.6	1.1	1.0	1.6
		15+ ^e	0.6 (1.5)	0.2	0.2	0.0	0.0	0.0	0.0	0.0	0.2	0.3	0.3	0.3
		15-24	0.2 (0.2)	0.8 (0.8)	0.1	0.5	0.0	0.0	0.0	0.0	0.1	0.6	0.0	0.6
		25-44	0.1 (0.0)	0.3 (0.1)	0.0	0.3	0.1	0.3	0.0	0.0	0.1	0.6	0.2	0.5
		45-64	0.0 (0.1)	0.1 (0.0)	0.0	0.1	0.2	0.0	0.1	0.0	0.1	0.3	0.2	0.2
B80 /1111	Iron deficiency /Iron deficiency anaemia	65-74	0.0 (0.0)	0.3 (0.0)	0.2	0.0	0.4	0.8	0.0	0.0	0.0	0.0	0.0	0.5
		75+	0.0 (0.3)	0.8 (1.0)	0.1	0.5	0.0	0.0	0.0	0.0	0.0	0.3	0.5	0.3
		15+ ^e	0.2 (0.2)	0.2	0.2	0.2	0.2	0.2	0.0	0.0	0.3	0.3	0.3	0.3
		15-24	0.7 (0.0)	12.6 (2.7)	0.3	4.7	0.3	8.5	0.0	0.0	1.1	11.4	0.9	4.5
		25-44	0.3 (0.2)	14.5 (2.2)	0.4	7.1	0.2	9.8	0.0	0.2	0.8	15.6	0.3	7.4
B81 /1101 & 1109	Pernicious or folate deficiency anaemia /Pernicious anaemia & other deficiency anaemia	45-64	1.1 (0.1)	7.7 (1.1)	0.8	5.7	1.6	8.0	0.3	0.4	2.2	9.4	1.1	5.3
		65-74	3.8 (0.4)	8.5 (0.7)	2.7	4.3	3.5	1.5	0.5	0.9	9.3	10.7	4.5	4.1
		75+	10.8 (1.0)	16.8 (2.2)	9.2	10.5	7.0	19.0	1.7	1.6	24.1	24.0	10.2	14.7
		15+ ^e	6.8 (1.0)	3.9	3.9	5.3	5.3	5.3	0.3	0.3	8.5	4.2	4.2	4.2
		15-24	0.0 (0.0)	0.0 (0.0)	0.0	0.2	0.0	0.0	0.0	0.1	0.1	0.5	0.3	0.3
T91 /0921	Vitamin deficiencies & other nutritional disorders /Vitamin deficiency	25-44	0.0 (0.0)	0.3 (0.1)	0.0	0.4	0.0	0.1	0.0	0.1	0.2	1.2	0.3	0.9
		45-64	0.2 (0.0)	0.5 (0.0)	0.2	0.5	0.4	0.1	0.1	0.0	1.0	1.6	0.3	1.0
		65-74	0.6 (0.0)	1.6 (0.2)	0.9	1.0	1.3	0.8	0.1	0.2	2.8	3.9	2.9	3.4
		75+	1.7 (0.0)	3.5 (0.4)	3.0	2.5	3.9	0.4	0.3	0.8	6.8	6.8	12.7	15.7
		15+ ^e	0.5 (0.0)	0.5	0.5	0.5	0.3	0.3	0.1	0.1	1.5	1.9	1.9	1.9
T08 /4570	Weight loss	15-24	0.2 (0.0)	0.3 (0.2)	0.0	0.3	0.0	0.3	0.0	0.0	0.0	0.1	0.0	0.1
		25-44	0.1 (0.0)	0.1 (0.0)	0.0	0.4	0.0	0.9	0.0	0.1	0.0	0.2	0.3	0.7
		45-64	0.5 (0.0)	0.2 (0.0)	0.2	0.4	0.1	0.4	0.1	0.2	0.2	0.1	0.5	0.7
		65-74	0.4 (0.2)	1.4 (0.0)	0.6	0.8	1.3	0.8	0.0	0.0	0.0	0.0	1.9	2.2
		75+	1.7 (0.0)	1.6 (0.2)	0.5	1.3	2.3	4.9	0.0	0.3	0.3	1.6	3.9	6.5
T08 /4570	Weight loss	15+ ^e	0.4 (0.0)	0.3	0.3	0.7	0.7	0.7	0.1	0.1	0.2	1.0	1.0	1.0
		15-24	1.5 (1.9)	4.1 (4.8)	1.3	2.3	0.6	0.6	0.0	0.2	1.8	2.0	1.3	3.3
		25-44	1.3 (1.7)	2.9 (3.6)	0.7	1.9	0.4	0.9	0.0	0.0	0.8	2.2	1.0	2.1
		45-64	3.1 (3.7)	2.5 (3.6)	1.0	1.7	0.2	0.1	0.0	0.2	1.5	1.9	2.2	2.4
		65-74	2.9 (4.0)	5.0 (7.1)	3.3	2.7	3.1	0.8	0.1	0.2	2.8	3.3	2.9	3.2
T08 /4570	Weight loss	75+	4.1 (5.4)	7.6 (8.4)	4.5	5.1	4.7	4.9	0.5	0.1	4.3	4.9	12.7	9.4
		15+ ^e	2.9 (3.6)	1.8	1.8	0.9	0.9	0.9	0.1	0.1	2.0	2.0	2.7	2.7

^aReasons for encounter rate (at start). ^bThe numerator is the number of episodes. ^cThe denominator is the 'mid-time' population (based on the mean of the population at start and at the end of the study period concerning size, age, gender and insurance type). ^dThe numerator is the number of patients with ≥1 'new' episode/problem. ^eStandardized (n/1,000) for the Dutch population during the observation years.

ICPC=International Classification of Primary Care; CMR=Continuous Morbidity Registration; RNG=Registration Network Groningen; RNH=Registration Network Family Practices; RNUH-LEO=Registration Network University Family Practices, Leiden and its environs; NS2=2nd National study.

Table 8 Prevalence (and reasons for encounter rate (total))^a (n/1,000 patient years) of registered nutritional deficiency related diagnoses for gender and preset age groups in Dutch general practice networks

ICPC/ E-list label (CMR)	Diagnosis	Age	Transition project ^b 1 Feb. 1985- 1 Jan. 1995		NS2 ^{c,d} 1 May 2000- 30 April 2002		CMR ^b 1 Jan. 1999- 31 Dec. 2003		RNH ^{c,e} 1 May 2000- 30 April 2002		RNG ^c 1 Jan. 1999- 31 Dec. 2003		RNUH-LEO ^b 1 Aug. 1998- 1 Aug. 2003	
			♂	♀	♂	♀	♂	♀	♂	♀	♂	♀	♂	♀
T03 /2920	Loss of appetite /Anorexia ecl. anorexia nervosa	years												
		15-24	0.9 (2.1)	1.1 (3.7)	0.2	0.6	0.0	0.0	0.4	0.1	0.0	0.4	0.2	0.3
		25-44	0.4 (1.0)	0.8 (2.2)	0.2	0.1	0.0	0.1	0.0	0.1	0.1	0.2	0.1	0.2
		45-64	0.4 (1.7)	0.5 (1.6)	0.1	0.2	0.0	0.0	0.0	0.0	0.1	0.2	0.2	0.1
		65-74	0.2 (2.5)	0.9 (5.3)	0.6	0.4	0.0	0.0	0.0	0.6	0.3	0.0	0.5	0.2
T05 /1061	Feeding problem adult /Nutritional disorders	75+	1.0 (5.4)	2.5 (6.6)	1.3	1.6	0.8	0.0	0.0	0.3	0.6	1.1	1.0	1.8
		15+ ^f	0.7 (2.4)	0.3	0.3	0.0	0.0	0.1	0.1	0.2	0.2	0.3	0.3	0.3
		15-24	0.2 (0.2)	1.1 (1.1)	0.1	0.6	0.0	0.0	0.0	0.1	0.1	0.6	0.0	0.7
		25-44	0.1 (0.0)	0.3 (0.1)	0.1	0.4	0.1	0.3	0.1	0.2	0.1	0.6	0.3	0.6
		45-64	0.0 (0.4)	0.1 (0.0)	0.1	0.2	0.0	0.0	0.3	0.2	0.1	0.3	0.2	0.4
B80 /1111	Iron deficiency anaemia /Iron deficiency anaemia	65-74	0.2 (0.2)	0.3 (1.0)	0.3	0.1	0.4	0.8	0.1	0.1	0.0	0.0	0.0	0.5
		75+	0.3 (1.4)	1.2 (2.0)	0.4	0.9	0.0	0.0	0.0	0.2	0.0	0.3	0.5	0.5
		15+ ^f	0.3 (0.4)	0.3	0.3	0.2	0.2	0.2	0.2	0.2	0.3	0.3	0.4	0.4
		15-24	1.0 (0.2)	14.2 (2.9)	0.7	0.3	0.3	8.5	0.1	1.0	1.1	11.9	1.0	5.3
		25-44	0.5 (0.2)	16.1 (2.8)	0.6	0.9	0.2	10.0	0.3	2.7	0.8	16.4	0.3	11.0
B81 /1101 & 1109	Pernicious or folate deficiency anaemia /Pernicious anaemia & other deficiency anaemia	45-64	1.2 (0.2)	10.9 (1.9)	1.7	1.2	1.9	8.6	1.5	6.2	2.2	10.0	1.2	9.6
		65-74	6.1 (1.9)	14.3 (5.2)	6.8	3.0	5.3	1.5	2.7	4.8	9.6	11.1	9.5	5.4
		75+	19.7 (6.4)	30.7 (13.5)	21.7	5.1	8.6	21.2	7.2	9.5	25.6	25.4	17.1	24.3
		15+ ^f	8.9 (2.2)	8.3	8.3	5.7	5.7	2.8	8.9	8.9	8.9	6.5	6.5	6.5
		15-24	0.0 (0.0)	0.0 (0.0)	0.0	0.6	0.0	0.0	0.0	0.1	0.1	0.5	0.5	0.7
T91 /0921	Vitamin deficiencies & other nutritional disorders /Vitamin deficiency	25-44	0.1 (0.1)	0.7 (0.1)	0.3	0.4	0.0	0.5	0.2	0.6	0.2	1.3	0.5	2.1
		45-64	0.6 (0.0)	1.3 (0.0)	1.3	0.2	0.8	1.5	0.6	1.5	1.1	1.7	2.1	4.4
		65-74	2.3 (2.8)	7.1 (4.1)	5.0	0.1	5.3	3.4	2.5	3.2	3.3	4.5	18.0	11.0
		75+	6.8 (7.9)	13.3 (12.3)	16.6	0.9	15.6	6.2	9.9	10.2	7.1	7.8	53.7	39.5
		15+ ^f	1.6 (0.8)	1.6	2.8	1.6	1.6	1.5	1.5	1.7	1.7	6.2	6.2	6.2
T08 /4570	Weight loss	15-24	0.3 (0.0)	0.3 (0.2)	0.1	0.3	0.0	0.3	0.2	0.0	0.0	0.1	0.1	0.1
		25-44	0.2 (0.0)	0.2 (0.0)	0.1	0.9	0.0	1.5	0.3	0.6	0.0	0.2	0.5	1.2
		45-64	0.8 (0.0)	0.4 (0.0)	0.6	1.2	0.2	1.6	0.4	0.2	0.1	1.2	1.4	1.2
		65-74	0.6 (0.2)	1.6 (0.0)	2.1	3.0	3.1	6.1	1.3	1.0	0.0	0.0	4.2	6.3
		75+	1.7 (0.0)	2.2 (0.2)	5.2	5.1	11.7	11.9	1.3	2.2	0.3	1.6	10.2	12.6
T08 /4570	Weight loss	15+ ^f	0.5 (0.0)	1.1	1.1	1.9	1.9	0.6	0.6	0.2	0.2	2.1	2.1	2.1
		15-24	2.1 (2.6)	4.1 (5.1)	1.8	2.8	0.6	0.6	0.2	0.1	1.8	2.0	1.4	3.4
		25-44	1.3 (2.0)	3.2 (4.6)	0.9	2.3	0.4	0.9	0.1	0.5	0.8	2.2	1.0	2.4
		45-64	3.2 (5.1)	3.0 (5.2)	1.4	2.3	0.2	0.1	0.3	0.4	1.5	1.9	2.5	2.7
		65-74	3.1 (4.8)	5.0 (9.1)	4.1	3.4	3.1	0.8	0.9	0.7	2.8	3.3	3.2	3.9
T08 /4570	Weight loss	75+	5.1 (8.1)	9.4 (12.7)	7.3	8.0	4.7	4.9	1.3	1.0	4.3	4.9	15.1	11.5
		15+ ^f	3.2 (4.7)	2.4	2.4	0.9	0.9	0.4	0.4	2.0	2.0	3.1	3.1	3.1

^a Reasons for encounter rate (total). ^b The numerator is the number of episodes. ^c The denominator is the 'mid-time' population (based on the mean of the population at start and at the end of the study period concerning size, age, gender and insurance type). ^d Point-prevalence. ^e Standardized (n/1,000) for the Dutch population during the observation years. ICPC=International Classification of Primary Care; CMR=Continuous Morbidity Registration; RNH=Registration Network Groningen; RNG=Registration Network University Family Practices, Leiden and its environs; NS2=2nd National study.



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PART ONE ||| CHAPTER 4

Weight loss in head and neck cancer patients little noticed in general practice

Journal of Primary Health Care (2009) accepted

Abstract

Introduction: In head and neck cancer patients, weight loss increases morbidity and mortality, and decreases treatment tolerance and quality of life. Early nutritional intervention has beneficial effects on these factors.

Aim: We observed patients' weight courses after specialists' care and surveyed nutrition related documentation by general practitioners (GPs).

Methods: From a Head and Neck Oncology Centre (HNOC) study, 68 patients were asked to participate in an extended general practice cohort. Twenty-six patients participated in the prospective three monthly weight measurements during the year after HNOC care. We extracted nutritional information contained in referral letters ($n=24$) and medical records from the year before referral ($n=45$) and after HNOC care ($n=26$). An impaired nutritional status was assigned to weight loss $\geq 10\%$ within six months or Body Mass Index (BMI) $< 18.5 \text{ kg/m}^2$ and 'at risk' to weight loss $\geq 5\%$ but $< 10\%$ within six months.

Results: Three (12%) participants were nutritionally impaired and two (8%) were deemed 'at risk'. Although GPs suspected a (pre-) malignancy in 11 cases (46%), only two (8%) documented weight loss or BMI and four (17%) nutrition related complaints in their referral letters. Medical records more often contained information on nutrition related complaints and tube feeding later in the disease course, as opposed to concern over weight loss or BMI.

Conclusion: Therefore, we call for nutritional management in general practice, by urging practitioners to assess patients' nutritional status throughout the disease course and intervene if necessary. The passing on of related information in case of referral promotes continuity of care.

What gap this fills

What we already know: Preventing weight loss in head and neck cancer patients decreases morbidity and mortality, but above all increases treatment tolerance and quality of life. In the hospital, 30-50% of the head and neck cancer patients are undernourished, and weight even further decreased during specialists' care.

What this study adds: GPs documented weight loss, BMI, nutrition related complaints or interventions in the minority of these patients, while the year after hospital care 20% was 'at risk' or nutritionally impaired.

Introduction

Nutritional deficiency ranges from micro- to multiple macronutrient shortages and results from physiologic (e.g. starvation) and/or pathologic conditions. Cachexia is such a complex pathologic hyper-metabolic condition defined by unintentional weight loss of greater than five percent of the premorbid weight within the previous six months.⁶ In general, the World Health Organization defines underweight as a Body Mass Index (BMI) $<18.5 \text{ kg/m}^2$.²⁹

Head and neck cancer patients are at evident risk for nutritional deficiency. Multiple factors undermine their nutritional status: a premorbid life style with poor dietary habits, often combined with excessive smoking and alcohol consumption,¹⁰⁹ the tumour location, which causes swallowing and food passage difficulties and finally the oncological treatment side effects.¹¹⁰

Weight loss in these patients increases morbidity and mortality and decreases treatment tolerance and overall quality of life.¹¹¹⁻¹¹³ Early and intensive nutritional intervention has produced beneficial effects on weight loss, quality of life and physical function in oncology outpatients receiving radiotherapy.¹¹⁴ Therefore, physicians should recognize and intervene early in cases of cachexia, starting with primary care, since in the hospital already 30-50% of the head and neck cancer patients are undernourished. The current practice by general practitioners (GPs) of tracing or intervening in case of cachexia, before referral and the necessity of additional care after hospital treatment, has never been studied.

Squamous cell carcinomas of the oral cavity, oropharynx and hypopharynx (OOH) are relatively rare: on average a Dutch GP sees a 'new' OOH carcinoma patient every five to ten years. However, GPs treat more cachexia related diseases in their practices, such as COPD and heart failure. Since the risk for nutritional deficiency in head and neck cancer patients is generally known, we chose this group to exemplify current nutritional management in general practice.

In a prospective, observational study performed at a Head and Neck Oncology Centre (HNOC), 22 of the 68 (32%) OOH cancer patients were 'at risk' for, or suffered from cachexia before treatment and their weight decreased even further during specialists' care.¹¹⁰

To illustrate the possible relevance and current nutritional management in general practice, we observed these patients' weight courses after HNOC care and surveyed documentation of weight loss, BMI, nutrition related complaints, and interventions by GPs the year before referral and after HNOC care.

Material and methods

Study frame

Between March 2004 and May 2005, after approval of the local Committee on Research Involving Human Subjects, we extended a study performed in a HNOC to general practice. Of the 150 consecutive newly referred patients with squamous cell OOH carcinoma, 116 were willing to participate. However, 68 patients met the inclusion criteria; age ≥ 18 years, primary tumour stage II-IV (UICC TNM-tumour classification),¹¹⁵ no history of malignancy and a primary curative treatment intent.^{110;116} At that time, all 68 patients signed an informed consent form for the use of their medical records.

Twelve patients already had died during oncological treatment in the HNOC. In the Dutch health care system patients are registered with one general practice, which supplies the professional medical care, including referrals to medical specialists. Therefore, we verified at general practices if patients were still alive, before asking them to participate. They received an informed consent form by mail, to authorize three monthly weight measurements during one year and/or the use of their medical records. We subsequently sent the signed consent forms to the cooperating GPs. Before each weight measurement, the participant received a reminder letter with a weight registration form and preprinted reply envelope. This form registered date, body weight (in kg) and dress (no or lightweight clothing, with/without shoes) and was filled out during each follow-up visit. For the 68 patients recruited in the HNOC, we looked up the primary referral letters available. We requested GPs to make available the medical record of participants and those who had died, from the year before referral and, if applicable, the year after HNOC care.

Main outcome measures

In the HNOC, body height and weight had been measured by a dietician with a Seca-stadiometer and Seca-weighing scales (in meters (two decimal) and kilograms (one decimal), respectively). During HNOC visits, questionnaires were filled out concerning nutritional information, such as energy (protein) supplements and tube feeding.^{110;116} After HNOC care, body weight was measured with GPs' weighing scales (in kilograms (one decimal)) and adjusted by 0.3 kg when the participant wore shoes. No correction for differences in dress were made.

We classified participants who lost ten percent or more of their previous weight within six months, or those with a BMI < 18.5 kg/m² at the final weight measurement, as nutritionally impaired. If they lost between five and ten percent of their previous weight within six months, they were classified as 'at risk' for an impaired nutritional status.

Documentation of information concerning the nutritional status in the referral letters and medical records were tallied and/or listed, also that related to co-morbidity. This included: weight loss or the BMI, nutrition related complaints – like swallowing or food passage difficulties – and interventions such as GPs' nutrition advice, energy (protein) supplements, treatment by a dietician and tube feeding (nasal passageway, Percutaneous Endoscopic Gastrostomy (PEG) or Percutaneous Radiological Gastrostomy (PRG)). The three monthly weight measurements documented in medical records were excluded, since these were not part of the usual care. The medical history, derived from medical records from the GPs and HNOC, was summed up to provide information on possible nutritional deficiency or fluid retention. Through referral letters, the differential diagnosis of the GPs was extracted.

Statistical Analysis

We analysed the data using the Statistical Package for Social Sciences (SPSS), version 12.0.1 (SPSS Corporation, Chicago, IL, USA). Characteristics of patients at intake and related documentation of the nutritional status in the referral letters and medical records were computed by frequency tables, and presented in numbers and percentages. The mean overall survival was the percentage of participants still alive from the date of intake in the HNOC, until the first weight measurement in general practice. Weight change (%) within follow-up intervals and BMI (kg/m²) at the final weight measurement were analysed and expressed by means with associated range and sd. With Chi-square we tested if differences occurred in documentation quantity of information within medical records before referral and after HNOC care. The latter was calculated including and excluding documentation related to co-morbidity. The level of significance was set on $p < 0.005$.

Results

Participants

Table 9 shows the main characteristics of the study population at HNOC intake.¹¹⁶ In decreasing order the tumour location was the oral cavity (53%), oropharynx (37%) and hypopharynx (10%). Of all patients, 37 had a tumour sized between two and four cm (T2), 19 had a tumour larger than four cm or any size (T3) and 12 of any size invading adjacent structures (T4). Most patients were treated by radiotherapy (37%), surgery (26%) or a combination of these two (22%). The remaining participants were treated by chemotherapy and radiotherapy. At the first HNOC visit, 23 (34%) patients used energy (protein) supplements, of which two were referred by the GP and 20 by specialists in regional hospitals or the HNOC. The one patient with tube feeding received the tube through another specialization within the HNOC.

Table 9 Characteristics of patients at intake at HNOC

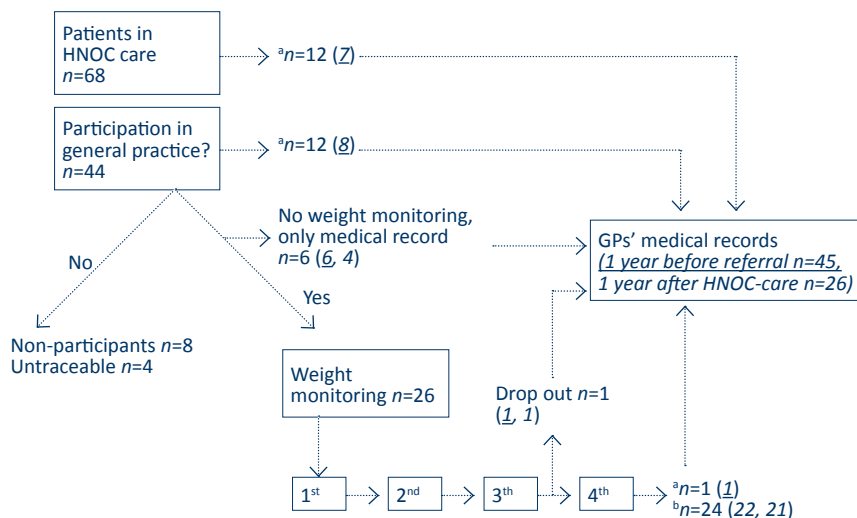
Variable		n (%)
Age (years)	30-60	39 (57)
	61-83	29 (43)
Tumour location	Oral cavity	36 (53)
	Oropharynx	25 (37)
	Hypopharynx	7 (10)
Tumour stage	T2	37 (54)
	T3	19 (28)
	T4	12 (18)
Treatment	Radiotherapy	25 (37)
	Surgery	19 (26)
	Surgery and Radiotherapy	14 (22)
	Chemotherapy and Radiotherapy	10 (15)
Energy (protein) supplements	Yes	23 (34)
	Not	45 (66)
Tube feeding	Nasal passageway	1 (2)
	No	67 (98)

T2=tumour between 2 and 4 cm; T3=tumour larger than 4 cm or any size; T4=tumour of any size, but invading adjacent structures.

Figure 4 presents the participant flow during HNOC and GPs' care. In total 24 patients died before the study was extended to general practice. The mean overall survival was 65% in one and a half year (range 0.9-2.0 years (sd 0.3)). Of the 44 patients remaining, eight declined participation, four were untraceable and six participated in the medical record analysis, but not in the weight monitoring. Finally, in total 26 participants were monitored. One participant dropped out during treatment because of another malignancy in her lungs. She was at risk for an impaired nutritional status

(7% weight loss in three months). Before referral, 45 participants' medical records could be analysed; of this number, 26 were available following HNOC care.

Figure 4 Participant flow during the HNOC and extended general practice study



^a Dead.

^b Alive.

Number of medical records one year before referral (in italics and underlined) and one year after HNOC-care (in italics).

Weight monitoring

Due to participants' personal and follow-up circumstances we were able to collect 53 of the 104 weight measurements. Among the 26 participants, ten had suffered or suffered from hypertension or other cardiovascular risk factors or diseases, four from myocardial infarction, five from alcohol abuse or related (chronic) diseases, five from digestive disorders, two from diabetes, two from gout, two from psychiatric disorders, two from another kind of cancer and one from hepatitis.

Table 10 displays the percentages of weight change after HNOC care. Two participants lost between five and ten percent of their previous weight in three months; one between the sixth and the ninth month, the other between the ninth and the twelfth month of follow-up. The first suffered from lung cancer (BMI 13.4 kg/m²) and the latter had an infection (BMI 23.6 kg/m²). None of the participants lost ten percent or more of their previous weight in three or six months. At the final measurement, the mean BMI was 23.5 kg/m² (n=25, sd 4.6, range 16.8-37.0 kg/m²) and three participants (12%) had a BMI<18.5 kg/m². In general, participants gained weight during follow-up intervals, ranging from a stable weight up to 2% weight increase.

Table 10 Percentages of weight change within follow-up intervals until one year after HNOC care

Variable	Follow-up interval (months)			
	0-3	3-6	6-9	9-12
n	4	4	9	14
Mean % weight change (sd)	2.3 (3.8)	0.0 (2.4)	1.8 (3.9)	0.3 (2.7)
Maximum % weight loss	3.2	2.5	7.0 ^a	6.7 ^a
Maximum % weight increase	4.8	3.2	5.0	4.5

^a 'At risk' for an impaired nutritional status (n=1).
sd=standard deviation.

Nutritional information

The GP referred 35 of the 68 (51%) participants. For 24 of them referral letters were available, in which two (8%) GPs documented weight loss or the BMI and four (17%) nutrition related complaints. In 11 (46%) cases a (pre-) malignancy was suspected.

Table 11 presents the GPs' documentation of weight loss or the BMI, nutrition related complaints and interventions in medical records. Before referral, 20% of the GPs reported weight loss or the BMI versus 16% after HNOC care. For nutrition related complaints and intervention this was 13% versus 19% and 7% versus 19%, respectively. There was no substantial difference observed in documentation of this information in medical records, before referral versus after HNOC care. Excluding documentation related to co-morbidity altered the results for nutrition related complaints and interventions; these were more frequently documented after HNOC care ($p=0.004$).

Table 11 General practitioners' documentation of the nutritional status, nutrition related complaints and interventions in medical records

Variable	Before referral (n (%))			After HNOC care (n (%))		
	Yes		No	Yes		No
	History	Measured		History	Measured	
Weight loss or BMI	4 (9)	5 (11) ^a	36 (80)	2 (8)	2 (8)	22 (84)
Nutrition related complaints ^c	6 (13) ^b		39 (87)	5 (19) ^c		21 (81)
Nutritional intervention ^f	3 (7) ^d		42 (93)	5 (19) ^e		21 (81)

^{a,b,d} Including cases due to co-morbidity ($n=1, 2, 4$, respectively).

^c Including cases with tube feeding ($n=2$).

^e Guidance by hospital dietician during treatment for lung cancer ($n=1$).

^f $p<0.05$ after exclusion of documentation related to co-morbidity.

Discussion

Patients remained vulnerable to an impaired nutritional status after specialists' care. In the minority of the patients, GPs documented weight loss or the BMI in referral letters and medical records before and after HNOC care. Although nutrition related complaints and interventions due to head and neck cancer were documented more after HNOC care, this was not the case for the assessment of patients' nutritional status by weight loss or the BMI.

This is the first in-depth analysis of GPs' documentation concerning the nutritional status. Although this study concerns only Dutch GPs, literature supports the need for nutritional attention in primary care in other Western countries.¹¹⁷⁻¹¹⁹

This study is limited, insofar, that the only parameters used to measure an impaired nutritional status were weight loss and the BMI. Weight loss could have been masked by fluid retention due to co-morbidity. No questionnaires or laboratory measurements have been performed to trace the actual occurrence of nutritional deficiency or other cachexia related changes, such as its inflammatory activity leading to catabolism of body cell mass.¹²⁰ The difficulty is that no uniform parameter exists to qualify the nutritional status. Another point is the limited number of participants, due to the rarity and poor survival rates of head and neck cancer. The mean overall survival in our study was representative; in literature two-year survival ranges from 50-65% for resectable^{121,122} and 23-26% for inoperable tumours.^{123,124} The three monthly weight measurements might have caused less weight measurements on the GPs' own initiative in usual care.

Our study has implications for daily practice. Co-morbidity can both cause a diminished nutritional status and result from it. For example, an infection can induce fever, anorexia and, as

a consequence, weight loss, or the infection can be the result of an impaired immune function due to a deficient nutritional intake.¹⁵ Optimizing patient's nutritional status, next to treating its causes or consequences, can prevent a vicious circle of negative occurrences. Therefore, mentioning swallowing or food passage difficulties and body weight or weight change in referral letters is important for early treatment of cachexia in hospitals. Since the GPs might have premorbid weight documentation, they can transmit valuable information to specialists. Specialists, in turn, should report nutritional information back to guarantee continuity of care.

In future research, more detailed nutritional information should be gathered by questionnaires, the occurrence of muscle mass depletion over time or even laboratory values in primary care patient groups at risk. Qualitative research in GPs on the awareness of cachexia and related thoughts could shed light on the current poor documentation.

In conclusion, we call for nutritional management in general practice by urging practitioners to assess patients' nutritional status in high risk groups throughout the disease course and intervene if necessary. Transferring related information in case of referral promotes continuity of care.

Acknowledgements

The Dutch Dairy Association funded this work. We thank all participants, GPs and specialists for their responses and participations, Nienke van der Veer for gathering the HNOC's medical records and Twanny Jeijnsman-Rouwhorst for her management skills.

Competing Interests

None declared.



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PART ONE ||| PARAGRAPH 4.1

Improving nutritional management within high risk groups

Abstract

The current pitfalls and future possibilities of nutritional management are discussed by two patients with tongue cancer who have suffered from substantial weight loss. Their nutritional problems are illustrative of those among other (cancer) patient groups. The main concerns are the lack of early case finding and dietary treatment, and insufficient nutritional information transfer through referral letters. The GP as a central and longitudinal caretaker faces challenges in improving nutritional management.

How this fits in

General practitioners provide care to many patient groups at high-risk for weight loss, such as those with cancer, Chronic Obstructive Pulmonary Disease (COPD), and chronic heart failure. Regular measurements of their body weight is essential for early intervention that may contribute to patients' quality of life.

Introduction

General practitioners care for many patients at risk for cachexia, in particular those with cancer, COPD, and chronic heart failure.⁸ Cachexia is a complex syndrome that combines anorexia, weight loss, and muscle and adipose tissue decline with weakness. Physicians often recognise cachexia only in the later stages and see it as an inevitable consequence of the disease. However, according to literature, cachexia should already be considered in case of unintentional weight loss of more than 5% within six months,⁶ especially since there is evidence that intervention can stabilise cachexia and improve quality of life. These interventions concern early individualised nutritional support with or without metabolic interference therapy.^{5;114} Nevertheless, the cancer stage generally forms the major determinant of a low quality of life.¹¹² Bio-impedance analysis or blood tests (for example, C-reactive protein and albumin levels) are some (additional) possibilities in diagnosing cachexia.^{8;120}

The aim of this paper is to illustrate the need for early management of cachexia and the barriers to doing so. Two case histories are presented, identified in a longitudinal observational study on weight loss in patients with head and neck cancer.^{110;125}

Case histories

The first patient was 61 years old when she visited her GP for a check-up of a painful spot on the tongue. The GP reported an ulcerative spot with a palpable lymph node in the neck. His hypothesis was an infection, or possible malignancy. After one week of antibiotic treatment, he referred her to the local hospital. Her medical history included irritable bowel syndrome, anxiety, and hypertension. The local specialist sent her to the head and neck oncology centre for specialised treatment. At the first visit to the centre she had a stable weight (60 kg, height 1.58 m (Body Mass Index (BMI) 24.0 kg/m²)) and received curative surgical treatment (tumour stage T1N1M0). She remained in good nutritional health during care at the head and neck oncology centre. In the following year, she suffered from a throat infection for which the GP treated her with antibiotics. According to the study's three monthly weight measurements, the patient lost 4.2 kg (6.7%) within three months, which the GP's record suggested was due to anorexia and nausea resulting from the infection and antibiotic side effects, as well as difficulties with her 'new' diet for recently diagnosed coeliac disease. No intervention had been undertaken.

The second patient was 83 years old, suffering from ulcerative colitis, depression and aortic stenosis. Her symptoms were persistent throat ache, which would radiate to the ear during swallowing. The GP noticed an irritated throat and sent her to the local hospital for further evaluation. His referral letter described odynophagia and he asked them to exclude pathology. The specialist diagnosed tongue cancer and sent her to the head and neck oncology centre. His referral letter documented the physical examination of the head and neck region. At the oncology centre polyclinic visit she had already lost 11 kg of her initial body weight (12%) in six months (formally 89 kg, height 1.72 m (BMI 30.1 kg/m²)). She received treatment through surgery and radiotherapy (tumour stage T2N0M0).

and received energy (protein) supplements. Her weight stabilised.

Discussion

Both patients are illustrative of the vulnerable nutritional balance in the chronically ill. The first patient lost weight due to multifactorial causes, triggered by an infection. The infection caused anorexia, resulting in weight loss. A diminished nutritional status, in turn, impaired her immune system, which led to the vicious circle of further weight loss and decline in resistance.¹⁵ The second patient lost more than 10% of her pre-morbid weight due to cancer, which is known to be an unfavourable prognostic sign.¹²⁶ Early intervention can only be realised by improving case finding with regular weight measurements. In these cases, nutrition related complaints were discussed between patient, GP, and/or specialist, but no objective measurement of (change in) body weight had been pursued, nor had body weight been reported in referral letters. This points to a lack of proactive orientation towards cachexia, as illustrated in the present study.¹²⁵

In order to include the prevention of weight loss in the care for patients at risk, it is essential to promote regular measurements of body weight before significant weight loss occurs, and to report them in case of referral or transfer of care. For cancer, COPD and chronic heart failure, patients' weight should be monitored regularly from the time of (possible) diagnosis, since early intervention in the case of cachexia may contribute to an enhanced quality of life.^{5;114}

Consent

The patients have consented to the publication of this report.

Funding body

The Dutch Dairy Association.

Ethics committee

The local Committee on Research Involving Human Subjects.

Competing interests

The authors have stated that there are none.

Acknowledgements

We thank the participants, GPs and specialists for their responses and participations.

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PART ONE ||| CHAPTER 5

Assessing nutritional depletion and its risk factors in COPD patients in general practice

Submitted for publication

Abstract

Background: Nutritional depletion worsens the overall prognosis of Chronic Obstructive Pulmonary Disease (COPD) patients. We established its prevalence in general practice and its association with COPD severity and aging, as well as predisposing factors.

Methods: Patients diagnosed with COPD were invited for spirometry, body height and weight assessment. They were included if they had a post-bronchodilator FEV1/FVC<0.70. By questionnaire, demographic, general practice and nutrition related items were gathered. In the elderly (>65 years), the Mini Nutritional Assessment (MNA) was administered additionally. We classified nutritional depletion as a Body Mass Index (BMI) <18.5, ≤21 kg/m² or MNA score <17 points and 'at risk' with a score between 17-23.5 points.

Results: After spirometry, 277 participants were enrolled of which 158 elderly. Of all participants, 7% and 11% had a BMI<18.5 and ≤21 kg/m², respectively. According to the MNA, 3 (2%) elderly were nutritional depleted and 23 (17%) were 'at risk'. No significant association was found between nutritional depletion, by a BMI<18.5 or ≤21 kg/m², and Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages or ageing. However, there was a trend of a decreasing mean BMI with increasing COPD severity group (p=0.020). Predisposing factors for (the risk of) nutritional depletion were difficulties in consuming meals, current smoking status and the use of drink supplements.

Conclusion: A substantial amount of primary care COPD patients was nutritional depleted. No apparent association with COPD severity or ageing was observed. Smoking cessation and meal instructions or adjustments possibly form an entry for intervention in COPD patients.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a slowly progressive, largely irreversible airflow limitation due to chronic inflammation and loss of the small airway structure. COPD is estimated to climb on the list of global leading causes of disease burden from the 13th place in 2004 up to the fifth place by 2030.¹²⁷ As the majority of COPD patients are to be treated in primary care, it is important to understand this evolving epidemic, which general practitioners (GPs) and other primary care providers will have to deal with. Of particular importance in this respect is responding to the complications of COPD.

One of such complications is the loss of mainly lean body mass (muscle tissue), also referred to as pulmonary cachexia. The consequences are a reduced functional capacity¹²⁸ and quality of life,^{24;25;129} but above all, an increased mortality risk independent of the COPD severity.^{17;31} Pulmonary cachexia is apparent in 20-40% of the patients with moderate to severe COPD.^{7;130} The exact pathogenesis remains obscure. Several underlying mechanisms have been postulated, such as side effects of medication (steroids), diminished nutritional intake, a hyper-metabolic rate, myolysis by inactivity, hypoxaemia/hypercapnia, oxidative stress, sympatic upregulation, inflammation, anabolic hormone insufficiency, altered leptin levels or a possible genetic predisposition.⁹

Besides pulmonary cachexia, ageing physiologically goes hand in hand with loss of muscle tissue, known as sarcopenia.^{11;12} So, sarcopenia may co-exist next to pulmonary cachexia in the elderly COPD patients. For this reason we use the overarching term nutritional depletion further on in this article. Although nutritional depletion is an important complication of COPD, there is only little information about its prevalence and predisposing factors in the primary care population.

The objectives of this study were to establish the prevalence of nutritional depletion in a general practice COPD population and to determine its association with COPD severity and ageing. We also explored demographic, general practice and nutrition related predisposing factors for nutritional depletion.

Methods

Study setting and population

This study was nested in a Randomised Controlled Trial (RCT)* concerning the effects of patient self-management on the outcome of COPD. Between June 2004 and November 2006, GPs from 15 practices in Nijmegen and surrounding recruited subjects aged 35 years and older registered as suffering from COPD. To support the recruitment, GPs were encouraged to (1) explore the problem lists of their Electronic Medical Records for the International Classification of Primary Care (ICPC) code R95; (2) review their list of the annual influenza vaccination campaign, and (3) evaluate their records of drug prescriptions. Before randomisation, GPs invited all selected patients for spirometry, body height and weight assessment. Initially, a questionnaire containing demographic, general practice and nutrition related data was performed, during the last phase of enrolment this questionnaire was minimized to enhance participation for the RCT and therefore nutritional items were left out. For those patients who were not invited, GPs were asked to elucidate the reasons of non-invitation. *www.clinicalTrials.gov, identifier: NCT00128765

Spirometry

Trained practice nurses or assistants performed spirometry if no lung function test was available from patients' medical records in the past two year. Spirometry was performed according to

American Thoracic Society criteria.¹³¹ All practices used MicroPlus or MicroLoop spirometers from MicroMedical Ltd. (Rochester, UK) with SpidaXpert 1.40 software. We calculated the post-bronchodilator Forced Expiratory Volume in one second (FEV1) of predicted according to Quanjer *et al.*¹³²

Patients were included if post-bronchodilator FEV1/Forced Vital Capacity (FVC)<0.70. COPD severity was categorised according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, i.e. stage 1 (mild airflow obstruction): predicted FEV1% $\geq 80\%$, stage 2 (moderate airflow obstruction): predicted FEV1% $\geq 50\%$ but $< 80\%$, stage 3 (severe airflow obstruction): predicted FEV1% $\geq 30\%$ but $< 50\%$ and stage 4 (very severe airflow obstruction): predicted FEV1% $< 30\%$.^{133;134}

Nutritional status

We provided all practices with calibrated Seca 888 digital weighing scales. During body weight measurements (in kilogram, one decimal), patients wore lightweight clothing without shoes. Body height was measured with a stadiometer (in meters, two decimals). The Body Mass Index (BMI) was calculated in kilograms per square meter. Practice nurses or assistants administered the Mini Nutritional Assessment (MNA). This questionnaire, which determines the nutritional status in the elderly (>65 years) by scored items, has been internationally validated in outpatient clinics, hospitals and nursing homes.¹³⁵ These items contain anthropometric measurements, questions regarding the dietary intake and a global assessment, see for more detail box 2.¹³⁶

Box 2

Mini Nutritional Assessment

contains 18 scored items concerning:

Anthropometric measurements

- BMI
- Mid-arm and calf circumference
- Weight loss

Questions regarding dietary intake

- Number of meals consumed
- Food/fluid intake and feeding autonomy

Global assessment

- Place of residence
- Medication
- Mobility
- Presence of acute stress, decubitus, dementia or depression
- Self-perception of health and nutrition

Patients were classified as being 'at risk' for nutritional depletion if the MNA score was 17-23.5 points and as nutritional depleted if the MNA score was < 17 points or the BMI was ≤ 21 kg/m².³¹ Since the World Health Organization defines underweight as a BMI < 18.5 kg/m²,²⁹ we also used this threshold to analyse the consistency of the results.

Demographic, general practice and nutrition related questionnaire

Initially, patients completed a questionnaire containing demographic, general practice and nutrition related items, such as date of birth, gender, place of residence, limitations in doing groceries, making and consuming meals, the use of Meals on Wheels services and concentrated drink supplements during the last month. It also contained items concerning side effects of all current medication used, treatment by dietician, physiotherapist and/or pulmonologist, the occurrence and number of hospital admissions in the last year and exacerbations in the last two years, as well as current or

former smoking habits. With the latter, pack years were calculated as the number of years smoked multiplied by the average number of cigarettes smoked per day, expressed as package(s) per day.

Statistical Analysis

We analysed the data using the Statistical Package for Social Sciences (SPSS), version 16.0.01 (SPSS Corporation, Chicago, IL, USA).

Descriptive statistics were calculated and differences between groups were compared by an unpaired t-test, analysis of variance (ANOVA) or Chi-square with a significance level set on 0.05.

To determine the association between nutritional depletion and sarcopenia, we divided patients into two age groups ≤ 65 and > 65 years, since literature reports higher prevalence rates of sarcopenia after the age of 60 to 70 years.^{11;12} We used logistic regression analysis to calculate the odds ratios (ORs) and their confidence intervals (CIs) of having a BMI ≤ 21 kg/m² or < 18.5 kg/m² between GOLD stage 1 versus 2; GOLD stage 1 versus 3 and 4; age group ≤ 65 versus > 65 years. ORs were calculated crude and with correction for age group or GOLD stage, gender and smoking.^{137;138}

Results

Patient recruitment

Overall, 1,386 (72%) of the 1,918 patients diagnosed as having COPD were invited for the study assessment in their general practice. The GPs did not invite the 532 patients for several reasons, e.g. deceased, moved or having severe co-morbidity. Of the 1,386 patients invited, 728 patients showed up to participate in the study. According to spirometry, 301 of these patients did not fulfil the GOLD criteria and 17 participants had incomplete spirometric data. In 133 subjects, the minimized questionnaire, without nutrition related items, had been used. Therefore these patients were excluded from further analyses. They did not differ in mean age ($p=0.233$), gender and GOLD stage distribution ($p=0.144$ and $p=0.266$, respectively), mean BMI ($p=0.078$) and proportion of those with a BMI < 18.5 or ≤ 21 kg/m² ($p=0.795$ and $p=0.054$) from the remaining 277 study participants used in further analysis.

Patients main characteristics

The mean age of the participants was 66.6 (sd 10.5) years, 67% of them were men. The distribution of GOLD 1, GOLD 2 and GOLD 3 and 4 stages was 22, 59 and 19%, respectively. The mean age and gender distribution did not differ within these GOLD staged groups. Table 12 displays the main characteristics of the COPD patients divided by BMI groups, ≤ 21 kg/m² versus > 21 kg/m². The mean age and proportion of elderly were comparable between these BMI groups.

Table 12 Main characteristics of the patients according to BMI group (BMI ≤ 21 kg/m² ($n=31$) and BMI > 21 kg/m² ($n=245$))

		BMI ≤ 21 kg/m ²		BMI > 21 kg/m ²		p-value
		Range	Mean (sd)	Range	Mean (sd)	
Age (years)		41-90	64.5 (11.9)	37-87	66.8 (10.3)	0.251
		<i>n</i>	%	<i>n</i>	%	
Age (years)	> 65	15	48.4	142	58.0	0.311
Gender	Women	18	58.1	74	30.2	0.002 ^{a,b}
COPD stages	GOLD 1	5	16.1	55	22.4	0.140 ^b
	GOLD 2	16	51.6	147	60.0	
	GOLD 3 and 4	10	32.3	43	17.6	

^a Significant.

^b Significant ($p < 0.05$) for BMI < 18.5 versus BMI ≥ 18.5 kg/m².

Nutritional depletion

Of all participants, 7% and 11% had a BMI<18.5 and ≤ 21 kg/m², respectively. In general, women more often had a BMI of <18.5 kg/m² or ≤ 21 kg/m² compared to men (7% versus 2% ($p=0.031$) and 20% versus 7% ($p=0.002$), respectively).

The mean BMI was lowest in (very) severe COPD patients (25.0 kg/m² (sd 4.7)) compared to those with mild and moderate airflow obstruction (26.9 kg/m² (sd 4.6) and 27.0 kg/m² (sd 4.6), respectively ($p=0.020$)). This was consistent in both men and women. More (very) severe COPD patients had a BMI<18.5 kg/m² compared to those with mild and moderate airflow obstruction (11% versus 2% and 1% of the cases, respectively ($p=0.001$)). For a BMI ≤ 21 kg/m² this difference was not significant ($p=0.140$).

From the 157 participating elderly, 3% had a BMI<18.5 kg/m² and 10% a BMI ≤ 21 kg/m². According to the 139 filled out MNA questionnaires, 17% of the elderly were 'at risk' and 2% nutritional depleted. Their distribution according to GOLD stages was: 6 elderly in GOLD 1, $n=12$ in GOLD 2 and $n=8$ in GOLD 3 and 4.

Table 13 presents crude and corrected ORs and their CIs of having a BMI ≤ 21 kg/m² between various groups. There was no association between a BMI ≤ 21 kg/m² and COPD severity or ageing. Correction for possible confounders, such as age or GOLD stage group, gender and smoking status did not alter the main results. When analyses were repeated for a BMI<18.5 kg/m² the results remained unchanged.

Table 13 Odds ratios of having a BMI ≤ 21 kg/m² within GOLD stage severity and age groups

Groups	OR crude	95% CI	OR corrected	95% CI
GOLD 2 versus 1	1.20	0.42-3.42	1.11 ^a	0.36-3.42
GOLD 3 and 4 versus 1	2.56	0.81-8.04	2.24 ^a	0.69-7.32
>65 y versus ≤ 65 y	0.68	0.32-1.44	1.05 ^b	0.47-2.38

^a Corrected for age group, gender and smoking.

^b Corrected for GOLD stage, gender and smoking.

General practice and nutrition related questions

According to the questionnaire, patients became more and more limited in doing groceries with increasing GOLD stage ($p=0.002$). (Very) severe COPD patients were most frequently treated by a physiotherapist or pulmonologist ($p=0.029$ and $p=0.001$, respectively). This was not the case for treatment by a dietician. In (very) severe COPD patients, the number of exacerbation in the past two years was higher compared to the other GOLD staged groups ($p=0.000$).

The elderly COPD patients more often lived alone ($p=0.042$), were more likely to have been hospitalized the former year ($p=0.016$) and were more often ex-smokers than current smokers compared to the younger patients ($p=0.009$).

In table 14 general practice and nutrition related items are listed for patients with a BMI ≤ 21 kg/m² and those with a higher BMI. COPD patients with a low BMI (<18.5 or ≤ 21 kg/m²) more often had difficulties in consuming meals ($p=0.000$ and $p=0.015$, respectively), were more frequently treated by a dietician ($p=0.029$ and $p=0.021$, respectively) and/or physiotherapist ($p=0.000$ and $p=0.000$, respectively) and were in the majority of cases current smokers ($p=0.002$ and $p=0.001$). Drink supplements were especially used in the BMI ≤ 21 kg/m² group ($p=0.002$), but not in the BMI<18.5 kg/m² group. The latter group was more often treated by a pulmonologist ($p=0.004$).

Table 14 General practice and nutrition related questions in the patients according to BMI group (BMI $\leq$ 21 kg/m 2 (n=31) and BMI>21 kg/m 2 (n=245))

		BMI $\leq$ 21 kg/m 2		BMI>21 kg/m 2		p-value
		n	Total n (%)	n	Total n (%)	
Place of residence	Alone	9	28 (32.1)	52	233 (22.3)	0.157
	With partner/family	18	28 (64.3)	180	233 (77.3)	
	Different than partner/family	1	28 (3.6)	1	233 (0.4)	
	Nursing home	0	28 (0)	0	233 (0)	
Doing groceries	Alone	28	30 (93.3)	216	236 (91.5)	0.618
	With help	2	30 (6.7)	13	236 (5.5)	
	Not at all	0	30 (0)	7	236 (3.0)	
Preparing meals	Alone	27	27 (100.0)	212	226 (93.8)	0.413
	With help	0	27 (0)	7	226 (3.1)	
	Not at all	0	27 (0)	7	226 (3.1)	
Consuming meals	No limitation	28	29 (96.6)	230	233 (98.7)	0.015 ^{a,b}
	Slight limitation	1	29 (3.4)	3	233 (1.3)	
	Severe limitation	0	29 (0)	0	233 (0)	
Meals on Wheels	Yes	1	30 (3.3)	7	236 (3.0)	0.912
Drink supplements	Yes	3	30 (10.0)	3	235 (1.3)	0.002 ^a
Peripheral oedema	Yes	0	30 (0)	20	232 (8.6)	0.094
Medication side effects	Appetite reduction	2	30 (6.7)	1	232 (0.4)	0.024
	Appetite enhancement	0	30 (0)	0	232 (0)	
	Nausea, vomiting or diarrhoea	1	30 (3.3)	5	232 (2.2)	
	Other	3	30 (10.0)	21	232 (9.0)	
Current treatment by	None	24	30 (80.0)	205	232 (88.4)	0.021 ^{a,b}
	Dietician ^c	7	30 (23.3)	22	235 (9.4)	
	Physiotherapist	4	30 (13.3)	3	236 (1.3)	
	Pulmonologist	12	30 (40.0)	56	238 (23.5)	
Hospital admission	Yes	5	30 (16.7)	29	236 (12.3)	0.499
Smoking	Non	2	30 (6.7)	23	236 (9.7)	0.001 ^{a,b}
	Former	8	30 (26.7)	139	236 (58.9)	
	Current	20	30 (66.6)	74	236 (31.4)	
		Range	Mean (n, sd)	Range	Mean (n, sd)	p-value
Hospital admission	n (in last year)	1-3	2.0 (4, 1.2)	1-6	1.5 (27, 1.2)	0.443
PAK years		0-57.0	24.1 (28, 16.4)	0-137.5	27.8 (205, 23.6)	0.430
Exacerbations/2 years		0-7	1.2 (31, 1.8)	0-9	1.1 (237, 1.4)	0.608

^a Significant.^b Significant (p<0.05) for BMI<18.5 versus BMI $\geq$ 18.5 kg/m 2 .^c Current or in the past.

The elderly 'at risk' or nutritional depleted according to the MNA also used more drink supplements (p=0.000), were more often treated by a physiotherapist (p=0.009), and were more often current smokers (p=0.006) or had been hospitalized more frequently during the last year (p=0.001).

Discussion

We demonstrated that at least ten percent of this primary care COPD population was 'at risk' or nutritional depleted according to a BMI $\leq$ 21 kg/m 2 or the MNA. Although a BMI<18.5 kg/m 2 occurred most often in (very) severe COPD patients, no statistically significant association was found between nutritional depletion, defined as BMI<18.5 or $\leq$ 21 kg/m 2 , and COPD severity or aging. Most consistent questions related to nutritional depletion, which could be relevant for intervention by a GP or practice nurse, were those concerning difficulties in consuming meals, current smoking status and the use of drink supplements.

Comparison to the literature

Up till now, only one study reported data in general practice concerning the prevalence of nutritional depletion in COPD patients.¹³⁹ The distribution of those with a BMI ≤ 21 kg/m² over the various GOLD stages were generally comparable, except our female population consistently showed higher rates. The higher prevalence of nutritional depletion in women was also observed in an outpatient study.¹⁴⁰

Compared to the Dutch general population, in which 2% of those aged 65 years and older had a BMI < 18.5 kg/m²,¹⁴¹ this study suggested a higher frequency of nutritional depletion in COPD patients. Although the number of patients in our study was very small.

In an out-patient centre study, age did not have any effect on the nutritional status, although not adjusted for possible confounders. They also did not observe a difference in the prevalence of nutritional depletion between GOLD stage 2 and 3, stage 1 and 4 were excluded from their study.¹⁴⁰

With the development of the Short Nutritional Assessment Questionnaire (SNAQ), a valid questionnaire for early detection of nutritional depletion in hospitals, the use of drink supplements was one of the most predictive questions of nutritional depletion, which also came forward in this study.¹⁴² We found that those nutritional depleted were in majority current smokers. Literature reveals evidence that current smoking induces or possibly accelerates sarcopenia.¹⁴³⁻¹⁴⁵ But in rheumatoid arthritis, another cachexia inducing disease, cigarette smoking has not been associated with a decrease in muscle mass, only with a reduced BMI.¹⁴⁶ In the general population, smoking is related to a lower weight and smoking cessation with weight gain.¹⁴⁷ A recently published study also reported slightly lower mean BMI in current smokers than never smokers, although the cigarettes smoked per day varied little with BMI.⁵⁰ In our study the number of PAK years also did not differ within the lower and higher BMI group. The authors suggested smoking intensity to be a confounder with BMI, since there is evidence that leaner smokers substantially have higher blood cotinine concentrations than other smokers.

Although hospitalization and exacerbation risk are reported to be higher in subgroups of underweight COPD patients,^{148;149} only a low MNA-score was a predisposing factor for hospitalization.

Methodological reflections

In this study moderate airflow obstructed patients were slightly overrepresented, compared to other data from the South¹³⁹ and the North West of the Netherlands.¹⁵⁰ Literature repeatedly positively correlates COPD severity with the occurrence of nutritional depletion. But in this study we did not consistently find such association, which can be due to the small number of (very) severe COPD patients in the primary care population.

A disadvantage of this study is that we did not determine the lean body mass by – for example – the Bioelectrical Impedance Analysis (BIA). The BMI does not differentiate between body fat and muscle mass, but is the most evidence based concerning the all risk and COPD mortality risk.^{17;50;57} Practically, the BMI is the most accessible tool in daily practice, next to unintentional weight loss, and provides additional information for other co-morbidities in general practice as well, as obesity. The MNA could be a more reliable tool in the elderly, since the decrease in body height with aging makes the BMI less reliable. The difficulty with the different nutritional assessment tools applied is how to interpret results, which is due to a lack of international consensus.

Recommendations for future research

A Cochrane review described that nutritional support in a non-pulmonary rehabilitation setting during only two to three months time showed no effect on anthropometric measures, lung function or exercise capacity in moderate to severe COPD patients.¹⁵¹ We postulate that COPD patients, as in the elderly, are less capable to recover once nutritional depleted.^{70;71} Early nutritional intervention studies in COPD patients in general practice should be performed to determine its effectiveness on quality of life, disease course and survival. Also the role of co-morbidity on the development of nutritional depletion in COPD patients is yet unknown, although most COPD patients suffer from multiple diseases with smoking as common origin.

General practice is in need for a more easy tool than the conventional BIA to trace muscle wasting,¹⁵² therefore cheaper but reliable alternatives should be explored. Also the usefulness, but above all the reliability of a leg-to-leg BIA or arm-to-arm BIA should be considered.

Conclusion

A substantial amount of COPD patients was nutritional depleted. No apparent association with COPD severity or ageing was observed. Smoking cessation and meal instructions or adjustments possibly form an entry for intervention in these patients.

Acknowledgement

We thank the Dutch Dairy Association for their financial support, Naomi Tillemans and Saskia Tabak for their contribution in the analysis, and Nicol Orbon and Riet Cretier for their data management skills.



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PART TWO ○○○ PARAGRAPH 5.1

Obesity in patients with COPD, an undervalued problem?

Franssen *et al* reported potential links between obesity and Chronic Obstructive Pulmonary Disease (COPD).¹⁵³ In their review, the authors use obesity prevalence estimates for COPD patient populations from only two studies with relative small sample sizes.^{139;154} Therefore, in our view, whether or not obesity is actually more prevalent in patients with COPD is still a matter of debate. Moreover, the current evidence on a possible association between obesity and worse COPD disease state is inconclusive. This information is crucial before considering any potential underlying mechanisms of this presumed association.

In order to contribute to the discussion on the role of obesity in COPD, we analysed data from a Dutch regional primary care diagnostic centre to address these questions. The procedures and database have been described elsewhere.¹⁵⁵ In short, our database contains spirometry tests of patients referred by general practitioners. Also information on Body Mass Index (BMI), smoking habits, exacerbation rate and level of dyspnoea (Medical Research Council (MRC) score) are collected during all visits.¹⁵⁵ For the current analysis, we used information from the most recent spirometric tests from all current and former smokers with respiratory symptoms aged >40 years and a post-bronchodilator forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) of <0.70. Body Mass Index (BMI in kg/m²) was categorised as low weight (BMI≤21), normal weight (21<BMI<25), overweight (25≤BMI<30), and obesity (BMI≥30). Obese patients were compared with normal and overweight patients in terms of post-bronchodilator FEV1% predicted, FVC and MRC scores. The association between obesity and these outcomes were analysed with linear regression and ordinal regression. The models were corrected for age, gender and current smoking habit.

Table 15 shows the characteristics of the study population ($n=1,761$) by BMI category. Overall, 15.1% of the study subjects were obese. FVC was 250 ml lower in obese patients compared to patients with normal weight and overweight ($p<0.01$). We found no association between obesity and post-FEV1% predicted, but obesity was associated with higher MRC scores (Odds Ratio (OR) 2.05, 95% CI 1.67-2.52).

Table 15 Characteristics of the study population by Body Mass Index (BMI) category

	Low weight BMI≤21 ($n=222$)		Normal weight BMI 21.01- 24.99 ($n=583$)		Overweight BMI 25-29.99 ($n=690$)		Obesity BMI≥30 ($n=266$)	
Age ^{a,b}	60.3	(11.2)	62.2	(10.7)	63.9	(10.3)	63.6	(10.0)
Gender (male)	104	(46.8)	363	(62.3)	497	(72.0)	168	(63.2)
Current smoker	154	(69.4)	331	(56.8)	289	(41.9)	111	(41.7)
GOLD stages								
1	32	(14.4)	89	(15.3)	91	(13.2)	22	(13.3)
2	100	(45.0)	362	(62.1)	440	(63.8)	187	(70.3)
3/4	90	(40.6)	132	(22.6)	159	(23.1)	57	(21.5)
MRC score								
0	55	(24.8)	211	(36.2)	215	(31.2)	46	(17.3)
1	92	(41.4)	238	(40.8)	277	(40.1)	114	(42.9)
2-4	75	(33.8)	134	(23.0)	198	(28.8)	106	(39.8)
Post-bronchodilator lung function								
FEV1% predicted ^a	56.5	(18.2)	63.0	(16.8)	62.7	(16.2)	61.1	(13.4)
FVC (l) ^a	3.2	(0.96)	3.4	(1.00)	3.4	(1.00)	3.1	(0.92)
FEV1/FVC ^a	0.54	(0.11)	0.57	(0.10)	0.59	(0.09)	0.62	(0.07)

Figures are number and percentage unless stated otherwise.

^a Mean (sd).

^b All differences between groups were significant ($p<0.01$).

The prevalence of obesity in our population was lower compared with the study by Steuten *et al* (i.e. 18%), but still slightly higher compared with the general Dutch population aged ≥ 45 .¹⁵⁶ Only the FVC was reduced in the obese COPD patients. This is an important observation, as this could result in underrepresentation of COPD in obese individuals when the main Global Initiative for Chronic Obstructive Lung Disease (GOLD) criterion (i.e. $FEV1/FVC < 0.70$) is applied to demonstrate airflow obstruction.

Although our findings indicate that the prevalence of obesity in patients with COPD is only slightly higher compared with that of the general population, obesity is a prevalent problem in patients with COPD associated with higher level of dyspnoea. Therefore, we ask for more attention to be paid to obesity in patients with COPD, in both research and patient care. Our efforts should not only focus on research into potential links between obesity and COPD, but also on effective ways to prevent and treat obesity in COPD patients, which may require a different approach from that in healthy subjects.



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PART TWO ○○○ CHAPTER 6

Encounters for common illnesses in general practice increased in obese patients

Family Physician (2008)25, Suppl 1, i93-8

Abstract

Background: Obese patients are known to have more chronic medical conditions.

Objective: To compare the frequency of encounter for episodes of the ten most common illnesses in general practice between obese and non-overweight patients.

Methods: Data were derived from the Continuous Morbidity Registration, containing data from four general practices in and around Nijmegen (the Netherlands). In this research and registration network, a matched cohort study was performed. Each obese patient (Body Mass Index ≥ 30 kg/m²), aged 20-75 years, was matched for age, gender, socio-economic status and general practice, to approximately two patients without the diagnosis 'overweight' or 'obesity'. Over a period of five years (January 1, 2000 to December 31, 2004), the frequency of encounter for episodes of the ten most common illnesses was compared, taking chronic medical conditions into account.

Results: At the start, 550 patients with obesity could be identified and were matched to 954 controls. Obese patients presented more common illnesses than non-overweight patients (incidence rate ratio 1.28, 95% confidence interval 1.12-1.47), in particular common cold (without fever), myalgia of the upper girdle, dermatophytosis and bruise (contusion, haematoma).

Conclusion: Obese patients present more common illnesses to their general practitioner, such as common cold (without fever), myalgia of the upper girdle, dermatophytosis and bruise (contusion, haematoma). This is in addition to their higher co-morbidity of chronic medical conditions.

Introduction

In industrialized countries, obesity is one of the greatest public health challenges of the 21st century. By 2010, one-fifth of Europe's population will be obese. So far, obesity accounts already for up to 6% of direct health costs in adults and more than 12% of indirect costs (shortened lives, reduced productivity and lowered incomes). With the growing prevalence of obesity, these costs will rise.¹⁵⁷

At the age of 40 years, obese patients have a decreased life expectancy of about seven years.⁴⁹ Obesity even accounts for 5% of all annual deaths in the European Union.¹⁵⁸ Excess weight is associated with number of other chronic medical conditions: hypertension, diabetes mellitus type 2 (DM 2), hyperlipidemia, heart diseases and certain types of cancer.^{42;45} Some share a common pathophysiology, but irrespective of the causal relation, they have an impact on functioning and health status.

A lower subjective health status and health-related quality of life have been reported in overweight and obese patients.^{52;53} This may (partly) explain why obese patients encounter the general practitioner (GP) more often than non-overweight patients.^{52;159-161}

We analysed if obese patients presented more episodes of the ten most common illnesses, not specifically obesity related, to the GP than non-overweight patients. Since obesity is linked to gender, age and social economic status (SES),^{162;163} which on their turn influence the use of health care,^{164;165} we wondered if there was an interaction within these variables.

Patients and methods

This study is a matched cohort analysis, comparing patients with obesity to non-overweight patients for the number of episodes of the ten most common illnesses presented to the GP during five years (January 1, 2000 to December 31, 2004). Obese and control patients were recruited from the Continuous Morbidity Registration (CMR) in and around Nijmegen, the Netherlands.¹⁰⁰

The CMR is a general practice research and registration network, which has operated since 1971. This database contains all morbidity episodes of the patients of four general practices in and around Nijmegen (ten GPs). From the start, every episode is classified and coded according to the 'E-list',¹⁰¹ the only general practice morbidity classification available at that time. To guarantee longitudinal research, the classification system has been maintained despite new developments. In time, diagnostic criteria have been introduced from the International Classification of Health Problems for Primary Care (ICHPPC), and other sources like guidelines.

The episodes are entered in the database linked to a patient-identity code, unique for every individual patient in the practices. The patient-identity code provides demographic characteristics; gender, age and SES. SES is grouped into low (unskilled and skilled manual workers), middle (lower employees) or upper class (higher employees), according to patient's occupation.¹⁶⁶

The data collection follows the principles of the Dutch health care system, in which everyone is registered with a GP and receives all medical care through that GP – including that of medical specialists after referral. Specialists report their diagnoses back to the GP, which are also included in the CMR database. In case an initial diagnosis has been changed, on the basis of observation, additional testing and/or referral, the corrected diagnosis is inserted in the database instead of the initial one.

In this study, all patients aged 20-75 years and registered with the diagnosis 'obesity' in the year 1999 were included. Obesity has been defined as a BMI ≥ 30 kg/m².²⁹ Each case was matched to approximately two controls from the practice lists who had not been diagnosed as 'obese' or 'overweight' (BMI ≥ 25 but < 30 kg/m²) between January 1, 1995 and December 31, 1999. Matching was performed for gender, age (± 4 years), SES and general practice of listing. We accepted changes in BMI class during follow-up in both the obese and control group.

Codes for chronic health problems are yearly automatically re-entered in the CMR database, or removed/changed by GPs if not present any more during a (non-related) encounter. For this reason we checked the diagnosis 'obesity' for the probability of misclassification in a random sample of the recruited patients ($n=227$). In the medical records we looked for recorded body weight and height to calculate BMI and categorized patients in 'overweight' and 'obesity'. This was based on the recorded measurement closest to January 1, 2000.

Statistical Methods

With SPSS (version 12.0.1), we tested possible differences within the main characteristics of the obese and overall CMR population by chi-square.

With the GENMOD procedure of SAS (version 9.1.3), we calculated incidence rate ratios (IRRs) for the ten most frequently presented common illnesses within the CMR database. These common illnesses comprised 32% of all illness episodes presented in general practice by these age groups. They were in descending order: common cold (no fever), nervous functional complaints (complaints with no somatic basis, but a psychosocial or functional one), myalgia upper girdle, dermatitis other (e.g. solar dermatitis, dyshidrosis, rhagades), dermatophytosis (candida infection, tenia pedis, pityriasis versicolor, dermatophytosis other), cerumen (wax in ear canal), urinary tract infection, bruise (contusion, haematoma), muscular skeletal symptoms other (e.g. pelvic tilt of unknown origin, contractures of unknown origin, epiphysiolysis, symphysiolysis, exostoses, non-structural abnormalities of the spine) and lumbago no radiating symptoms. The IRR has been calculated by the number of new cases of a common illness per obese during follow-up divided by the number of new cases of a common illness per control during follow-up.

We assumed a negative binomial distribution. Confidence Intervals (CIs) were corrected for over- and underdispersion. Analyses were adjusted for matched factors (gender, age, SES, general practice) and co-morbidity of chronic medical conditions. The latter was done as there is a higher possibility to present a common illness during follow-up encounters for chronic medical conditions. These chronic medical conditions adjusted for included asthma, DM 2, heart failure, hypertension and chronic bronchitis (Chronic Obstructive Pulmonary Disease).¹⁶⁷

The analyses for the combined ten most common illnesses presented were based on their cumulative episodes and were done separately for gender, age and SES group. Tests for interaction were performed to trace differences in IRRs within these groups.

Results

Five hundred fifty patients with the diagnosis 'obesity' were identified on January 1, 2000. They could be matched to 954 non-overweight patients. The mean age was 50.8 years in the obese (range 20-75 years) and 50.0 years in the control group (range 20-77 years).

Of the 1,504 patients (mean follow-up 4.6 years (standard deviation (sd) 1.1)), 1,286 (86%) could be followed for five years. Reasons for follow-up of less than five years were death (21 (4%) in the obese versus 31 (3%) in the control group) and patients moving out of the practice region (49 (9%) versus 126 (13%)).

In 90% of the random sample in the obese group ($n=204$), the BMI could be calculated from the available data in medical records. This sample comprised eight misclassified patients (4%), who were according to our calculations in fact overweight. The mean BMI was 34.8 kg/m^2 (sd 5.1, range 26.2-67.8). In 38 patients (7%) of the total obese group, the diagnosis had been reclassified as 'overweight' during follow-up, while 38 patients (4%) of the total control group were recoded as 'overweight' and 19 (2%) as 'obese'.

Table 16 presents the main characteristics of the obese and control group in comparison to the total CMR population. The obese patients were more likely to be female, aged 40 years and older, and belong to the low SES class ($p=0.00$, $p=0.01$ and $p=0.00$, respectively).

Table 16 Main characteristics of the obese and control group compared to the total CMR population

		Obese		Controls		CMR	
		n^a	%	n^a	%	n^a	%
Gender	Male	192	35	354	37	4,633	50
	Female	358	65	600	63	4,726	50
Age (years)	20-39	143	26	263	28	3,783	40
	40-64	300	55	516	54	4,577	49
	≥ 65	107	19	175	18	999	11
SES ^b	Low	318	58	524	55	3,362	37
	Middle	204	37	374	39	3,955	42
	Upper	28	5	56	6	1,664	18
Total		550	100	954	100	9,359	100

^a Number of person years (mean from January 1, 2000 to December 31, 2004).

^b Containing missing data.

Table 17 displays the ten most frequently presented common illnesses in the CMR database and the frequency of encounter adjusted for matched factors (gender, age, SES, general practice and co-morbidity of chronic medical conditions). When additionally adjusted for chronic medical conditions, obese patients presented more common colds (without fever), myalgia of the upper girdle, dermatophytosis and bruises (contusion, haematoma) than the controls. Taking the ten most common illnesses all together, there was a 28% higher presentation by obese patients (95% CI 1.12-1.47).

Table 18 shows the frequency of encounter for the combined ten most common illnesses presented, separately for gender, age and SES group. There was no difference within gender, age and SES group ($p=0.39$, $p=0.11$ and $p=0.85$, respectively).

Table 17 The frequency of encounter for an episode of the ten most common illnesses within the CMR database

Common illnesses		<i>n</i> ^a		Corrected ^b		Corrected ^c	
		Obese	Controls	IRR	(95% CI)	IRR	(95% CI)
1.	Common cold (no fever)	352	396	1.51 ^d	(1.22-1.88)	1.40 ^d	(1.11-1.78)
2.	Nervous functional complaints	160	255	1.07	(0.84-1.38)	1.10	(0.81-1.48)
3.	Myalgia upper girdle	236	257	1.45 ^d	(1.12-1.87)	1.52 ^d	(1.18-1.94)
4.	Dermatitis other ^e	207	264	1.28 ^d	(1.01-1.62)	1.13	(0.89-1.44)
5.	Dermatophytosis ^f	98	83	1.75 ^d	(1.36-2.25)	1.83 ^d	(1.36-2.45)
6.	Cerumen (wax in ear canal)	156	254	1.06	(0.69-1.63)	1.15	(0.78-1.68)
7.	Urinary tract infection	225	235	1.33	(0.93-1.92)	1.12	(0.78-1.60)
8.	Bruise (contusion, haematoma)	151	175	1.47 ^d	(1.11-1.96)	1.40 ^d	(1.04-1.89)
9.	Muscular skeletal symptoms other ^g	129	187	1.17	(0.90-1.52)	1.14	(0.87-1.49)
10.	Lumbago no radiating symptoms	126	178	1.21	(0.95-1.54)	1.17	(0.90-1.53)
	Cumulative	1,840	2,284	1.31 ^d	(1.15-1.50)	1.28 ^d	(1.12-1.47)

^a Number of episodes.^b Corrected for gender, age, SES and general practice.^c Corrected for gender, age, SES, general practice and the presence of chronic medical conditions (asthma bronchial, diabetes mellitus type 2, heart failure, hypertension, chronic bronchitis).^d Significant.^e For example: solar dermatitis, dyshidrosis, rhagades.^f For example: candida infection, tenia pedis, pityriasis versicolor, dermatophytosis other.^g For example: pelvic tilt e causa ignota (e.c.i.), contractures e.c.i., epiphysiolysis, symphysiolysis, exostoses, non-structural abnormalities of the spine.

Table 18 The frequency of encounter for the combined ten most common illnesses presented within the CMR population, separately for gender, age and SES group

		<i>n</i> ^a		Corrected		p-value ^b
		Obese	Controls	IRR	(95% CI)	
Gender	Male	500	674	1.19	(0.94-1.52)	0.39
	Female	1,340	1,610	1.34 ^c	(1.15-1.56)	
Age (years)	20-39	430	563	1.45 ^c	(1.14-1.85)	0.11
	40-64	1,070	1,195	1.43 ^c	(1.18-1.73)	
	≥65	340	526	1.00	(0.77-1.30)	
SES	Low	1,156	1,340	1.21	(1.00-1.46)	0.85
	Middle	614	818	1.37 ^c	(1.13-1.67)	
	Upper	70	126	1.43	(0.84-2.45)	

^a Number of episodes.^b Test for interaction.^c Significant.

Discussion

Obese patients presented 28% more of the ten most common illnesses to their GP, in particular common cold (without fever), myalgia of the upper girdle, dermatophytosis and bruise (contusion, haematoma). There was no difference within gender, age and SES group.

Comparison of literature

Our results are confirmed by literature. Frost and Lyons¹⁶¹ also found an increase of encounter by obese patients of 30% ($p=0.005$), after adjustment for the number of co-morbidities amongst others. Van Dijk *et al*¹⁵⁹ additionally reported the most profound diseases by organ systems this accounted for, of which musculoskeletal and skin problems were common illnesses. They also reported higher prescription rates for dermatologicals, drugs for musculoskeletal and respiratory system (e.g. antibiotics). Another study of the Counterweight Project Team draw equal conclusions.¹⁶⁸ Our study, however, focused specifically on the most presented common illnesses, which has never been described before. Even in children these trends are also observed.¹⁶⁹

The underlying relation between obesity and the common illnesses found in this study remains

obscure. In literature, a link between obesity and immune function alterations has been reported.¹⁷⁰ However, in this study obese patients only presented more common colds (without fever), but not more other infectious diseases as urinary tract infections. Therefore, this pathophysiological phenomenon does not totally explain these results. Also the higher presentation of musculoskeletal pain of the neck and shoulder remains unclear, since it is questioned if obese patients present more pain in general.¹⁷¹⁻¹⁷³ Perhaps only the lower suboptimal subjective health objectified in obese patients plays a role in the increased GP consultation, since this consequently results in obtaining more diagnoses for one or other (common) illness. But whether weight reduction in obese patients leads to better subjective health remains unknown.

Methodological reflections

This study was performed in a longitudinally constructed database, the CMR,¹⁰⁰ which facilitates longitudinal research of individual patients' medical history. Within the CMR, GPs organize regular feedback meetings to optimize inter-GP agreement in coding morbidity. The validity of long-term CMR morbidity recording has been satisfactory.¹⁷⁴ This is in line with the check for misclassification of the diagnosis 'obesity', in which little mistakes occurred. The prevalence of obesity within the CMR (6.5%) was equal to that reported by other data from in and around Nijmegen.¹⁷⁵ In 1977, within the CMR general practices, the BMI of 80% of all patients aged 20-50 years had been routinely measured for research purposes.¹⁷⁶ In 1994, a follow-up study took place, in which BMI again was measured.¹⁷⁷ Normally, body weight are measured on request of patient or GP and routinely in known high-vascular risk groups. So it cannot totally be ruled out that some controls wrongfully have no 'overweight' or 'obesity' diagnosis. Case finding in daily practice is initially performed 'at sight' and then objectified. This likely skews the overweight distribution towards obesity. If a GP measures body weight, a patient is more likely to be too thin or too fat. Also in 1977, higher cutoff points for overweight were used (BMI $\geq$ 26 kg/m² for women and BMI $\geq$ 27 kg/m² for men);¹⁷⁶ therefore we did not include patients with overweight in our analyses.

Some patients who were initially obese eventually became overweight during follow-up, and those non-overweight were diagnosed later on as 'overweight' or 'obese'. Exclusion of 'borderline' obese or weight cycling patients might influence results, since the effect on the consultation for common illnesses is unknown. As shown in our data, it concern a minority of patients. Moreover, it is more representable for common practice to include these patients.

In the control group though, more people left the general practice and this might have overestimated the reported frequency, since a shorter follow-up time subsequently might have decreased the number of the presented episodes of illnesses.

Workload GP and prevention

In the Netherlands, 10% of the adult population was obese between 2000-2003.¹⁷⁵ From this data, we assume that an average Dutch GP took care of 248 obese patients. In that case, our results suggest that a GP had an increased workload of 33 episodes every year due to common illnesses presented by obese patients, besides the routine encounters for obesity related co-morbidity of chronic conditions, such as hypertension and DM 2. The increase in workload of the GP has also been stated by others.¹⁵⁹⁻¹⁶¹

According to our findings, GPs have more opportunities to weigh obese patients regularly and intervene. But GPs believe that obesity management is primarily the responsibility of the patient.¹⁷⁸ Nevertheless, obesity eventually affects their own workload, and therefore prevention and timely

treatment may have benefits for the GPs as well as the patients. Regular weight measurements might give a warning signal.

Conclusion

Obese patients present more common illnesses to their GP, in particular common cold (without fever), myalgia of the upper girdle, dermatophytosis and bruise (contusion, haematoma). This is in addition to the higher prevalence of chronic medical conditions related to obesity.

Acknowledgements

Contributorship statement—CAMvW: Protocol development, drafting of manuscript. MBTL: Protocol development, article development (editing). AHvR-S: Protocol development, article development (editing). JHJB: Data collection and analyses. JCB: Protocol development, article development (editing). WAvS: Article development (editing). CvW: Guarantor, article development (editing). JJvB: Protocol development, article development (editing).

Declaration

Funding: Dutch Dairy Association.

Ethical approval: None.

Conflicts of interest: None.

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PART TWO ○○○ PARAGRAPH 6.1

Community care versus individual care in family practice

In her article,¹⁷⁹ Lucy Candib argues for a syndemic orientation towards what is currently one of the largest public health challenges: excess body weight. Candib calls for action from clinicians (in particular family practitioners (FPs)) to use community-strategies to counteract the overweight epidemic caused by multiple factors.

We support her notion that FPs can play a vital role in this epidemic, ranging from individual guidance, through – if achievable – initiating local community-based projects. In this commentary, however, we would like to emphasize that FPs predominantly provide weight management in high risk groups, such as diabetes patients. In many countries, the continuity of care in family practice provides an ideal basis for long-term intervention beyond only high-risk groups.¹⁸⁰ Furthermore, patients perceive FPs to be knowledgeable and reliable sources of lifestyle information and want FPs to have a role in weight management. Although busy day-to-day schedules leave FPs little time for such activities outside the core business,¹⁸¹ initiatives for multiprofessional teams to provide weight management services can bring relief on the long-term.¹⁸²

It may be very disappointing and/or discouraging for individual FPs to put large efforts into community-based activities outside their offices and to see little or no effect in the patients inside their offices. Since community-based approaches take a very long time to grow and their impact, while modest (at best) on the community level,¹⁸³ varies largely among individuals. Also obesogenic factors like the food industry and fast-food trends are not likely to be changed by FPs.

So we urge FPs and other health professionals to take an active role. However, we strongly believe that it is most realistic to call for action from FPs as fore fighters inside their offices, on an individual/family level, and as supports on community level. In the end, change can only be made by individuals themselves, and exactly in this area FPs can contribute most.



CHAPTER 7 || 0

General discussion

Table 19 Main findings of the studies described in this thesis

Goal	Design	Population	Main findings
Nutritional deficiency/undernutrition			
<i>Background information</i>			
Overview of prevalence and clinical assessment tools of ND in literature (chapter 2)	Review	All/specific groups, ≥ 18 years	In 8 studies, prevalence ranged between 0 to 13% within heterogeneous populations and had been obtained by different clinical assessment tools
Prevalence of ND in research and registration networks (chapter 3)	Cohort, follow-up 2-10 years	General, ≥ 15 years	Iron deficiency anaemia was the most incident and prevalent documented; ND had mostly been documented in the elderly; ND had little been documented and not registered separately from the underlying disease
<i>In-depth analysis in 'high risk' groups</i>			
1. Prevalence assessment of nutritional impairment by BMI and weight loss 2. Nutrition related documentation by GPs (chapter 4)	Retrospective and prospective cohort, follow-up 1 year	Head and neck cancer, retrospectively $n=45$, prospectively $n=26$	1. During the year after HNOC-care, 12% of the participants was nutritional impaired and 8% 'at risk' 2. In referral letters, 8% of the GPs reported weight loss or BMI, for nutrition related complaints this was 17%; In medical records, GPs reported more nutrition related complaints and tube feeding 1 year before referral than up till 1 year after HNOC-care, but weight loss or BMI had been equally documented
1. Prevalence assessment of nutritional depletion by BMI and MNA and association COPD severity and aging 2. Assessment of predisposing factors (chapter 5)	Cross-sectional	GOLD 1-4 and ≥ 35 years, $n=277$	1. Approximately 10 to 20% of the patients were 'at risk' and/or nutritional depleted; There was no significant association between nutritional depletion and COPD severity or aging 2. Predisposing factors for (the risk of) nutritional depletion were difficulties in consuming meals, current smoking status and the use of drink supplements
Obesity			
<i>Disease/illness related</i>			
Role of obesity in COPD (paragraph 5.1)	Cross-sectional	GOLD 1-4, current and former smokers, >40 years, $n=1,761$	Obese patients had a reduction of FVC with 250 ml and a higher level of dyspnoea (OR 2.05 (95% CI 1.67-2.52))
Frequency of encounter for the 10 most common illnesses; obese versus non-overweight patients (chapter 6)	Matched cohort, follow-up 5 years	20-75 years, matched for age, SES and general practice, $n=550$ cases versus $n=954$ controls	IRR 1.28 (95% CI 1.12-1.47); Obese patients presented more common colds (without fever), myalgia of the upper girdle, dermatophytosis and bruises (contusions, haematomas)

ND=Nutritional Deficiency; BMI=Body Mass Index; HNOC=Head and Neck Oncology Centre; GP=General Practitioner; COPD=Chronic Obstructive Lung Disease; MNA=Mini Nutritional Assessment; GOLD=Global Initiative for Chronic Obstructive Lung Disease; FVC=forced vital capacity; OR=Odds Ratio; CI=Confidence Interval; SES=Socio Economic Status; IRR=Incidence Rate Ratio.

General discussion

The main objective of the first part of this thesis was to describe the frequency of nutritional deficiency/undernutrition in the adult general practice population and in specific patient groups at risk for undernutrition. Knowledge of 'high risk' groups promotes in general the feasibility of prevention and this knowledge is widely used in daily general practice care. We performed a systematic review and described data from research and registration networks, as well as from two studies in patients with head and neck cancer and Chronic Obstructive Pulmonary Disease (COPD), respectively. Additionally, we summarized the clinical assessment tools used, since no universal agreement exists in the reliability and applicability of these tools. The studies obtained more insight in the current nutritional management of general practitioners. In the second part of this thesis, we especially focused on the health effects of obesity and the implications for daily practice. To specify, it contains two letters to the editor and a study in which we explored the frequency of encounter for the ten most common illnesses in general practice. The main findings of the thesis are summarized in table 19.

PART 1 The occurrence and current practice of nutritional deficiency/undernutrition

Conclusions

According to the literature review (chapter 2, table 5) and the other two studies presented in this thesis (chapter 4 and chapter 5), the prevalence of (the risk for) undernutrition in 'at risk' groups is approximately 10 to 40%. Another observation was that undernutrition was hardly diagnosed or identified in daily practice. General practitioners often did not register nutritional deficiency/undernutrition as a separate diagnosis (chapter 3 and chapter 4), despite its negative consequences on patients' quality of life, morbidity and mortality risk. As well, we noticed a lack of proactive involvement of general practitioners in undernutrition – even in patients at obvious risk for undernutrition, as head and neck cancer patients (chapter 4 and paragraph 4.1). For example, referral letters and medical records contained little information on nutrition related complaints, and even less on weight loss or the Body Mass Index (BMI).

Reflections

Only a few studies have been published on the frequency of undernutrition in general practice.^{18;32;73-78;139} All of them lack large study samples, which makes adjusting for confounders difficult or even impossible. This was the case in the study concerning head and neck cancer patients, but also for the study on COPD patients (table 19). Although we observed a trend of a decreasing mean BMI with increasing COPD severity, there was no significant association between nutritional depletion (by BMI group) and COPD severity.

Despite this drawback, this thesis provides more information to a relatively underexplored subject in primary care. Most literature on undernutrition concerns the hospital setting or nursing homes. A difficulty in health care related research is not only the difference in setting, but also the difference in its organization between countries. For instance, in the UK and the Netherlands, patients are registered with a general practice and the general practitioner is the gatekeeper. In other countries patients can easily switch from one general practice to another and specialists can be consulted without general practitioners' referral. This makes comparing of studies – as we did in chapter 2 – difficult, since there is no common denominator to calculate incidence, prevalence and other frequencies. The more comparable the systems, the more confident data can be compared

(chapter 3, 4, 5 and 6). The different patient groups studied reflect the great diversity in the primary care population.

As came forward in the literature review, another issue that impedes comparison of studies, is the lack of a uniform assessment tool for undernutrition. In the reviewed studies the clinical assessments used were: (1) the Body Mass Index (BMI), with or without triceps skin-fold thickness or mid-arm muscle circumference, (2) presence of weight loss or (3) the Mini Nutritional Assessment (MNA), a validated questionnaire. Literature concerning hospital studies describe even more clinical assessments, such as Dual-Energy X-ray Absorptiometry (DEXA), the Bioelectrical Impedance Analysis (BIA) and laboratory values.^{22;120} The ones that are accessible for general practice are also discussed for its clinical application in the next paragraph. In the two studies, in which we assessed the nutritional status, we also applied different tools: the BMI, combined with weight loss or the MNA (table 19). The nature of this choice was mainly the difference in study setting; a prospective cohort is suitable for identifying both BMI and weight change in time, while a cross-sectional study limits these possibilities. Therefore in chapter 5, the BMI and the MNA were used. Furthermore, the BMI, weight loss or the MNA can easily be applied in general practice, and therefore patients were expected to be more willing to participate.

Of all the available clinical assessments for undernutrition, the BMI has been most extensively linked to the mortality risk. But change in body weight, especially unintentional weight loss reflects a negative energy balance better than a single determined BMI. Firstly, because the BMI is less reliable in the elderly, due to the age related height loss. Secondly, also obese patients are undernourished when they have lost a substantial amount of weight unintentionally. Thirdly, a low BMI may reflect a genetic slender predisposition instead of undernutrition in those patients with a sufficient healthy balanced food intake and stable body weight during adult life.

But fluid retention can mask weight loss and this could have influenced our results in the cohort study of head and neck cancer patients. Questionnaires or laboratory measurements should be considered in such cases. Though blood samples, such as (pre-) albumin, Hb, CRP, can have additional value in case of cachexia,¹²⁰ they are unspecific and therefore not advisable for routine use in our view. Fluid retention also makes the application of the BIA untrustworthy. The BIA is commonly used to estimate the muscle mass in COPD patients treated in hospitals. In this patient group, research shows that muscle mass depletion determines mortality and not the loss of fat mass.^{31;152;184} The use of the BIA in other patient groups should be further explored in research, as well as possible (cheaper) alternatives (e.g. leg-to-leg or arm-to-arm BIA). This is relevant, since it is unclear if merely the loss of muscle mass is important for survival, or also the loss of adipose tissue in case of a normal muscle mass. This will probably vary between different diseases.¹⁸⁵

The value of the mid-upper arm circumference is currently being researched and might be a better indicator for the mortality risk than the BMI in the elderly.¹⁸⁶ The mid-upper arm circumference is much more practical to use in home care than body weight measurements. Other anthropometric measurements, such as the skin-fold thickness still must be further validated.¹²⁰ Nutrition screening or assessment questionnaire can also be useful, for example the MNA. But many of these questionnaires are too time consuming for daily practice. According to nutrition experts, questions of the loss of appetite or reduced food intake are important to identify a diminished nutritional status, in the context of a consultation.¹⁸⁷ In our cross-sectional study in COPD patients, we identified comparable predisposing factors, such as difficulties in consuming meals and the use of drink supplements.

We suggested a lack of proactive involvement in undernutrition, on the basis of the analysis of patients' medical records. Qualitative research could give a better insight in the awareness and in choices made by general practitioners and patients in the management of cachexia related diseases.

In conclusion, the origin of the lack of universal agreement on clinical assessment tools for undernutrition, as well as on its definition, is the complex and (yet) unravelled genesis of cachexia, sarcopenia and in a lesser extend wasting/emaciation. Currently, the best feasible tool for the routine use in general practice is unintentional weight loss, followed by the BMI. Monitoring body weight is important, especially since many common diseases – of which guidelines have been developed – relate to both undernutrition and weight gain, as illustrated in table 2. In the fragile elderly, other easy screening tools are of great value as an alternative for the sometimes impractical weight measurements in home care.

PART 2 Health effects of obesity and consequences for daily practice

Conclusions

The growing prevalence of obesity will have a strong impact on patient care, as illustrated in COPD patients (paragraph 5.1). The workload of general practitioners will increase, not only because of routine encounters for obesity related co-morbidity of chronic conditions,¹⁵⁹⁻¹⁶¹ but also by an increase of 28% for the ten most common illnesses (chapter 6). These common illnesses were: common colds (without fever), myalgia of the upper girdle, dermatophytosis and bruises (contusions, haematomas). General practitioners, together with other health care professionals, should play a more active role in the obesity epidemic by providing evidence based weight management for patients with and without an increased cardiovascular risk.⁶² This may urge general practitioners to engage in projects outside the traditional setting of their offices, and initiate local community-based projects (paragraph 6.1).

Reflections

In the matched cohort study concerning the frequency of encounter for common illnesses (chapter 6), the follow-up was five years. In these years some obese patients had become overweight and some non-overweight controls had been diagnosed as overweight or obese later on. Since general practitioners do not routinely measure body weight and height, a few patients in the control group might have been overweight or obese. This could have negatively influenced the results, so we advise to keep the diagnosis as 'pure' as possible, especially in research focussing on finding a pathological link between obesity and illnesses or diseases.

One of such links found in obesity is an altered immune function.¹⁷⁰ Adipose tissue has been described as an immune active organ.⁴⁰ The effect of obesity on the susceptibility for infectious diseases – as we found for common colds (without fever) – is worth further exploring, in those patients without nutritional deficiency, in for example flu epidemics. Its physiology might even shed a light on the effect of a diminished fat mass, as in most cases of undernutrition.

Proposed role of the general practitioner

Since malnutrition becomes more prevalent in the community, the general practitioner faces many challenges ahead in nutritional management, both for undernutrition in specific 'at risk' groups as well as for an excess body weight beyond those with an increased cardiovascular risk.⁶² Though still

much research in this field is necessary to obtain evidence based nutritional intervention methods, general practitioners could already bring nutrition into their interaction with the patient more often than they currently do.¹⁸⁸ Particularly with malnutrition becoming more relevant in the community, it is not possible for daily practice to wait for better scientific evidence: pending this, general practitioners must act on their collective experience, clinical wisdom and consensus. In this view, we propose the following role the general practitioner could fulfill with the dilemmas. Currently, the pitfall is that nutritional needs are often hidden in the complexity of other health issues and are likely to be overlooked and undermanaged in clinical practice unless explicitly addressed.¹⁸⁹

Prevention and treatment: the ideal situation

The most important of all, treatment should fit the individual patients' needs, beliefs and problems. Ideally, for the prevention or early treatment of undernutrition and an excess body weight, regular weight measurements should be performed, also in those patients visiting the general practitioner for other reasons. This accounts for all elderly, overweight and obese patients, but especially for those with symptoms or a diagnosis related to malnutrition. With a slight unintentional decrease ($\geq 5\%$ but $< 10\%$ within half a year) or increase of the body weight, patients will be more easily motivated to turn the tide with specific nutrition advices, often combined with adequate physical activity. Firstly, the reason for the disturbed weight balance should be explored and secondly – if necessary – further intervention should take place, such as additional tests or referral. If the nutrition advices do not reach their realistic goal or weight change is already substantial, nutritional intervention is needed in close collaboration with a dietician. Often a physiotherapist is necessary to pursue an increase or stabilization in muscle strength to preserve daily life activities. Preventing obesity is less difficult than treating it. Once a patient is obese, a moderate weight loss of 10% over a prolonged period of time is a realistic goal and already has beneficial health effects.^{58;190} If not achievable, patients should at least be encouraged to stabilize their weight. In general, besides determining the body weight, the waist circumference is of additional value, particularly in those with a normal weight or overweight. With a high waist circumference also non-obese patients should be motivated to increase their level of physical activity. A multidisciplinary setting, as mentioned in the last paragraph, forms the best treatment in case of malnutrition.^{5;39}

The majority of general practitioners classify encounters by International Classification of Primary Care (ICPC) codes in their electronic medical patient records. In chapter 3 and chapter 4 we noticed that patients more often presented the symptom weight loss or other nutrition related complaints, than the general practitioner diagnosed undernutrition as a stand-alone health problem or performed weight measurements, respectively. Most likely, nutrition related complaints were merely symptoms of a possible underlying disease and therefore the nutritional status fades into the background. By labelling undernutrition as ICPC-code T08 (weight loss or cachexia) and an excess body weight as T83 (overweight) or T82 (obesity), the awareness for these issues in the next encounter can be increased. This could be achieved by including the earlier mentioned ICPC-codes, in a new ICPC domain of risk factors, next to symptoms and health problems/diagnoses. In case of referral, mentioning body weight and weight change in time is important to guarantee the continuity of care. Especially in case of undernutrition, also since in Dutch hospitals screening of the nutritional status in newly submitted patients has become a benchmark.

Dilemmas in prevention and treatment

Conditions in primary care are optimal for giving nutrition advice, but general practitioners do not always capitalize on their excellent position – for which lack of time, training in nutrition and patients' poor compliance with dietary prescriptions are held responsible.^{191;192} 'The time-factor' should be

placed in the perspective of continuity of care: patients consult their general practitioner often over longer periods of time. This allows for helping to make and retain major changes over a number of consultations, rather than a one-off shot. Nutrition input in undergraduate and specialty training should be increased, especially which dietary advice to prescribe and how to communicate it.^{193;194} General practitioners need more knowledge on the background and possibilities for treatment of undernutrition and to a lesser extent on obesity: obesity has been described much more in literature than undernutrition. Management of obesity is something doctors tend to avoid, because it is much easier to prescribe for instance lipid lowering drugs than trying to persuade someone to eat less. Therefore, training in specific communication skills can be helpful to promote patients' behavioural change, one example is the patient centered approach.¹⁹⁵ Another issue is that the collaboration between the general practitioner and dietician can still be improved.

It is doubtful if universal prevention of obesity belongs to the primary care field. General practitioners are forced to focus their work and make the best use of limited time and resources. However, those patients with undernutrition or obesity related diseases (see introduction) are to a large extent under the general practitioners' care. Here weight management is part of the overall treatment and management and if patients or caretakers reject treatment, they should at least repeatedly be motivated (comparable to smoking cessation). The practice nurse or assistant can play an important role in tracing undernutrition or an excess body weight (or high waist circumference), since he/she already treats most patients in at risk groups for malnutrition, such as those with COPD, hypertension, diabetes mellitus 2 or heart failure.

Important in weight management is the own responsibility of patients or their care takers. It is necessary to supply information about the health consequences of the nutritional disorder they have or are 'at risk' for. Additionally, these patients need to be supported with individual nutritional advice, if necessary and proper instructions on the frequency of the body weight measurements, together with clear instructions when to contact the general practitioner or practice nurse. The regular weight measurements in general practice serve as an example and aim to start intervention in early stages, especially in vulnerable patients who sometimes lack own responsibility or care. The negative side of regular weight measurements perhaps can be that patients who are not satisfied with their body weight, will constantly be confronted with it, which can cause resistance or incidentally eating disorders in susceptible subjects.

Just like smoking cessation, obesity treatment often has poor long-term efficacy and effectiveness, which may be attributable to barriers on part of patients and health care professionals.¹⁹⁶ Barriers on the general practitioners' part can be his/her attitudes and beliefs, since also general practitioners tend to stigmatize their obese patients as awkward, unattractive, ugly and non-compliant.^{197;198} In this context, web-based health behaviour change programmes may be a successful alternative in weight management,¹⁹⁹ although the Counterweight Project Team from the UK has developed an effective intervention strategy to tackle an excess body weight based on a two year follow-up.⁵⁵ This strategy was used to make an intervention strategy for Dutch general practitioners, named the minimal intervention strategy (MIS).⁵⁶ The MIS seems very promising, but still needs to be tested further on its usefulness and effectiveness in daily practice in the future. We want to stress that obesity is a chronic disease, which needs lifelong treatment.

Also in case of ideal weight management in general practice, the obesity epidemic will not disappear until the wider society, politics and economics and education give it priority.¹⁹³ But general practitioners can increase awareness, since patients highly value general practitioners' knowledge

and reliability of lifestyle information.¹⁸¹ In case of cachexia, nutritional intervention is eventually limited. However, proper nutritional care can still enhance the quality of life.^{5,114} Therefore, weight management is just a part of the complete treatment, although not always mentioned in related guidelines of the Dutch College of General Practitioners. At this moment the Dutch College of General Practitioners is implementing undernutrition in relevant guidelines and developing a separate guideline for obesity.

For the general practitioner with a special interest in nutrition

The involvement of general practitioners in public health initiatives cannot be taken for granted. However, general practitioners can form a link between other health care professionals, community and the government. The primary care field therefore can play an essential role in broader intervention strategies. One example is the prevention of overweight and especially obesity in children. Overweight children have a two- to fourfold increased risk of becoming an overweight adult compared to children with a normal weight.²⁰⁰ Above all, already 92% of the obese children have one or more cardiovascular risk factor.²⁰¹ General practitioners can participate in local community-based projects, such as interventions in schools. These kind of multidisciplinary interventions seem promising.^{202,203} Still this requires political support and long-term investment.²⁰⁴ This kind of health care promotion can be seen as an integral part of service deliveries of the health care sector and can be an important contribution to the containment of rising health costs. Koelen *et al* described factors which are important in achieving and sustaining collaboration between public health/health promotion and individual medical care.²⁰⁵

In the scope of undernutrition, a unique opportunity to weigh a large group of patients 'at risk' is during the annual influenza vaccination campaign. In the Netherlands, these patients are 60 years and older and/or have specific co-morbidity. What possible practical implications this has and the prevalence of undernutrition are being explored at the end of 2009.

Past, current and future developments

In 1995, the Heelsum Collaboration on General Practice Nutrition was founded. This is a group of scientists in the field of general practice, epidemiology, methodology, nutrition, health promotion and communication, as well as researchers interested in the interface between nutrition education and medicine in general practice. Once every three year, these experts discussed ways of helping general practitioners to use nutrition in a more appropriate way in their work with patients with evidence based nutrition advice and counseling as its objective.

One of their initiatives is the development of the Diet and Nutrition Working Group of the Cochrane Primary Health Care Field. The Cochrane collaboration is an organization dedicated to making up-to-date, accurate information about the effects of healthcare interventions by high quality systematic reviews. The Diet and Nutrition Working Group is challenged in the way that evidence based nutrition needs more than randomized controlled trials (RCTs). RCTs are often not suitable, nor realistic, to determine the effect of nutritional intervention, for example in case of avoiding vegetables in a large group of people for five years to see if these people develop cancer.²⁰⁶ Most existing evidence base in nutrition is observational, mostly prospective cohort studies, which can be compiled in non-randomized systematic reviews. Also these kinds of reviews have many methodological pitfalls and as a consequence restrictions.²⁰⁷ Systematic reviews, which can be relevant for general practitioners to use during encounter, will be summarized into the Practical Evidence About Real Life Situations (PEARLS).²⁰⁸

An enormous force behind developments in the undernutrition field is the Dutch Malnutrition Steering Group. For home care and general practice settings, they recently developed a quick and easy screening tool for the elderly (Short Nutritional Assessment Questionnaire 65+ (SNAQ⁶⁵⁺)). For residential homes, the Short Nutritional Assessment Questionnaire Residential Care (SNAQ^{RC}) is available.²⁰⁹ The Dutch Malnutrition Steering Group will perform a prospective study on the health effects and cost effectiveness of early nutritional management in general practice. All of this is performed to implement an evidence based programme for home care organizations and general practices.

The best treatment for patients with undernutrition and obesity is provided in a multidisciplinary setting. The core team consists of a general practitioner and/or practice nurse, dietician and often a physiotherapist, together with a district nurse in case of undernutrition and a psychologist in case of obesity.³⁹ In the future this close collaboration in primary care is important to manage malnutrition. In this thesis, we showed that the general practitioner and/or practice nurse should play a key role. The general practitioner is most trusted and provides the long-term (evidence based) care with the best insight into the personal, medical and social environment of a patient.



CHAPTER 8 || 0

Summary

Summary

Since in the near future the prevalence of undernutrition – by an increased number of fragile elderly – and overweight/obesity will rise, general practitioners will more frequently face their (health) consequences (chapter 1). This thesis aims to clarify the importance of nutrition advice for general practitioners in the prevention and treatment of undernutrition and obesity. In part one, the main aim was to explore the frequency of nutritional deficiency in the adult general practice population, excluding eating disorders. Additionally, we obtained more insight into the current management of undernutrition by general practitioners. The second part of this thesis was dedicated to link obesity to (health) consequences in general practice from a single chronic disease (Chronic Obstructive Pulmonary Disease (COPD)) to multiple common illnesses and the implications for daily practice.

PART 1 The occurrence and current practice of undernutrition

In chapter 2, we performed a systematic review on reported prevalence and clinical assessment of nutritional deficiency in primary care studies. We derived articles from MEDLINE, Current Contents and EMBASE until 2003. Two independent reviewers determined the quality of the articles that met the inclusion and exclusion criteria. We included eight studies, which contained methodological flaws, especially selection bias. The prevalence ranged from 0 to 13% depending on the study population and clinical assessment used. The populations studied varied from the ill or elderly patients to the overall general practice population. Clinical assessments used were: (1) the Body Mass Index (BMI), with or without triceps skin-fold thickness or mid-arm muscle circumference, (2) presence of weight loss or (3) the Mini Nutritional Assessment (MNA), which is a validated questionnaire.

Since literature was rare, we explored incidence and prevalence rates of nutritional deficiency in the adult general practice population in chapter 3. Six Dutch general practice research and registration networks supplied these data for the diagnoses – classified by the International Classification of Primary Care (ICPC) or ‘E-list’ – ‘loss of appetite, feeding problem adult, iron, pernicious/folate deficiency anaemia, vitamin deficiencies and other nutritional disorders and weight loss’. We asked these networks whether disease related nutritional deficiency was registered separately from the underlying disease. This was the case in two of the six participating networks, although no clear difference in their reported incidence and prevalence rates could be observed. ‘Iron deficiency anaemia’ had the highest incidence (0.3-8.5/1,000 patient years) and prevalence (2.8-8.9/1,000 patient years) rates, followed by ‘weight loss’ (0.4-3.2 episodes/problems per 1,000 patient years) and ‘pernicious/folate deficiency anaemia’ (1.5-6.2 episodes/problems per 1,000 patient years), respectively. Generally, nutritional deficiency was mostly diagnosed in the elderly. According to the literature, we expected a higher percentage of patients with a nutritional deficiency related diagnoses than reported by the networks. So, we concluded that nutritional deficiency was little documented in general practice and generally not registered separately from the underlying disease.

Therefore in chapter 4, we assessed the nutritional status of patients with head and neck cancer and surveyed nutrition related documentation in the referral letters and medical records by their general practitioner. An impaired nutritional status was assigned to weight loss $\geq 10\%$ within six months or $\text{BMI} < 18.5 \text{ kg/m}^2$ and ‘at risk’ to weight loss $\geq 5\%$ but $< 10\%$ within six months. During the year after treatment in the Head and Neck Oncology Centre, three (12%) participants were nutritionally impaired and two (8%) were ‘at risk’. Referral letters from general practitioners reported a suspicion of a (pre-) malignancy in 11 cases (46%), while only two (8%) comprised information

on weight loss or the BMI and four (17%) nutrition related complaints. Also medical records more often contained information on nutrition related complaints and tube feeding later in the disease course, as opposed to that of weight loss or BMI. Although the number of patients in this study was very small, it suggested that general practitioners lack a proactive approach towards cachexia. Paragraph 4.1 is a case report of two patients from this study.

Chapter 5 concerns a more common disease in general practice, namely COPD. Due to the cross-sectional nature of this study, we assessed the nutritional status by the BMI and in the elderly by the MNA. Of all 277 participants, 6.5% and 11.2% had a BMI <18.5 and ≤ 21 kg/m², respectively. According to the MNA, 23 (16.5%) of the 158 elderly were 'at risk' and three (2.2%) were nutritional depleted. We also established the association of nutritional depletion with COPD severity and aging, as well as predisposing factors. Although these associations were not significant, there was a trend of a decreasing mean BMI with increasing COPD severity group (by Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage 1 to 4). Predisposing factors for (the risk of) nutritional depletion were difficulties in consuming meals, current smoking status and the use of drink supplements. Therefore, we concluded that smoking cessation and meal instructions or adjustments possibly form an entry for intervention in these patients.

PART 2 (Health) effects of obesity and consequences for daily practice

Paragraph 5.1 shows that obese patients with COPD had a reduced forced vital capacity (FVC), which increased the main GOLD-criterion (i.e. post-bronchodilator forced expiratory volume in one second (FEV1)/FVC < 0.70). Consequently, obese patients were possibly underrepresented. Also obese patients experienced an increased level of dyspnoea.

We described the role of obesity in the frequency of encounter for episodes of the ten most common illnesses in general practice in chapter 6. This study showed that the 550 obese patients presented more common illnesses to their general practitioner than the 954 matched non-overweight controls over a five year period (incidence rate ratio 1.28, 95% confidence interval 1.12-1.47). This was the case for the common illnesses: common cold (without fever), myalgia of the upper girdle, dermatophytosis and bruise (contusion, haematoma), independent of the presence of chronic medical conditions. Together with the routine encounters for obesity related co-morbidity of chronic conditions, the workload in the primary care field will increase further in the future.

Paragraph 6.1 contains a letter on the possible role of the general practitioner in the obesity epidemic.

The main conclusions of these studies are discussed in chapter 7, together with the reflections and proposed role of the general practitioner and the various dilemma's that may occur. Especially for the general practitioner with a special interest in nutrition, a broader scope of (universal) prevention has been written. General practitioners can expand their task beyond their office. We summarized a few developments concerning malnutrition of which general practitioners can profit in the future.



PARAGRAPH 8.1 || 0

Samenvatting

Samenvatting

In de nabije toekomst zal het aantal patiënten met een verslechterde voedingstoestand – mede door de vergrijzing – en met overgewicht/obesitas stijgen. Hierdoor zullen huisartsen in toenemende mate met de gerelateerde (gezondheids) consequenties te maken krijgen (hoofdstuk 1). In dit proefschrift beschrijven we de mogelijkheden en noodzaak van preventie van deze energie disbalans ‘uitersten’ in de huisartsenpraktijk. Het eerste deel behandelt voornamelijk het vóórkomen van een verslechterde voedingstoestand bij volwassenen in de huisartsenpraktijk, met exclusie van eetstoornissen, zoals anorexia nervosa en boulimia nervosa. Deze studies gaven ons tevens meer inzicht in het huidige beleid van huisartsen. Het tweede deel van dit proefschrift bevat studies naar enkele (gezondheids) consequenties van obesitas op een chronische ziekte (Chronisch Obstructief Longlijden (COPD)) en meerdere alledaagse klachten.

DEEL 1 Het vóórkomen van een verslechterde voedingstoestand en het huidige beleid

Hoofdstuk 2 bevat een systematische review, waarin we de prevalentie van een verslechterde voedingstoestand en gebruikte diagnostische criteria in de huisartsenpraktijk onderzocht hebben. Uit MEDLINE, Current Contents en EMBASE selecteerden twee onafhankelijke beoordelaars, op basis van in- en exclusie criteria, artikelen tot het jaar 2003. Zij beoordeelden de artikelen op vooraf bepaalde kwaliteitskenmerken. Acht studies werden geïncludeerd, met allen een matig tot slechte kwaliteit. De prevalentie varieerde van 0 tot 13% afhankelijk van de onderzoekspopulatie – (chronisch) zieken, ouderen of de algemene huisartsenpopulatie – en de diagnostische criteria: (1) de Body Mass Index (BMI) met of zonder triceps huidplooïdikte of spieromtrek van de bovenarm, (2) aanwezigheid van gewichtsverlies tot (3) een gevalideerde vragenlijst genaamd ‘de Mini Nutritional Assessment’ (MNA).

Omdat weinig literatuur beschikbaar bleek te zijn, vroegen we de Nederlandse huisartsenregistratie netwerken om incidentie en prevalentie cijfers van voedingsdeficiëntie gerelateerde diagnosen – volgens de International Classification of Primary Care (ICPC) of ‘E-lijst’ –, waaronder ‘verminderde eetlust, voedingsproblemen volwassene, ijzerebreksanemie, pernicieuze/foliumzuur deficiëntie anemie, vitamine-/voedingsdeficiëntie, gewichtsverlies/cachexie’ (hoofdstuk 3). We vroegen aan deze zes netwerken of de diagnosen apart van het onderliggend lijden werden geregistreerd. In twee netwerken was dit het geval, echter geen duidelijke verschillen in de incidentie en prevalentie cijfers waren waarneembaar. ‘Ijzerebreksanemie’ had de hoogste incidentie (0,3-8,5/1 000 patiëntjaren) en prevalentie (2,8-8,9/1 000 patiëntjaren), gevolgd door respectievelijk ‘gewichtsverlies/cachexie’ (0,4-3,2 episoden/problemen per 1 000 patiëntjaren) en ‘pernicious/folate deficiency’ anemie (1,5-6,2 episoden/problemen per 1 000 patiëntjaren). Over het algemeen kwamen voedingsdeficiëntie gerelateerde diagnosen meer voor bij ouderen. Omdat deze cijfers veel lager waren dan die van de systematic review, concludeerden we dat een verslechterde voedingstoestand zelden los geregistreerd werd van het onderliggend lijden in de huisartsenpraktijk.

Om deze reden hebben we in hoofdstuk 4 de voedingstoestand van patiënten met hoofd-, halskanker vastgesteld tot een jaar na behandeling in een universitair ziekenhuis. Een slechte voedingstoestand werd geclassificeerd als een gewichtsverlies van $\geq 10\%$ in zes maanden of $\text{BMI} < 18,5 \text{ kg/m}^2$ en risico hierop als een gewichtsverlies $\geq 5\%$ maar $< 10\%$ binnen zes maanden. In het jaar na behandeling in het universitair ziekenhuis raakten drie (12%) patiënten in een slechte voedingstoestand en twee (8%) verkeerden in de risico zone. Daarnaast hebben we documentatie gerelateerd aan de voedingstoestand in verwijsbrieven en het medisch dossier van de huisarts nagetrokken, zoals de

differentiaal diagnose, symptomen die de voedingstoestand zouden kunnen verslechteren (onder andere slikklachten), gewicht(sbeloop), BMI en eventuele voedingsadviezen of behandelingen. Volgens de verwijfsbrieven dacht de huisarts bij 11 patiënten (46%) aan kanker of een voorstadium hiervan, terwijl slechts in twee (8%) brieven informatie over gewichtsverlies of BMI en in vier (17%) verwante symptomen vermeld stond. De medische dossiers bevatten meer informatie over verwante symptomen en sonde voeding een jaar na behandeling in het universitair ziekenhuis dan een jaar vóór verwijzing, terwijl gewichtsverlies of de BMI niet vaker werden gedocumenteerd. Hoewel de onderzoekspopulatie klein was, geeft deze studie weer dat huisartsen niet proactief denken in het geval van cachexie. Paragraaf 4.1 beschrijft in meer detail twee patiënten met een slechte voedingstoestand uit deze studie.

Hoofdstuk 5 betreft een minder zeldzame ziekte in de huisartsenpraktijk. In dit dwarsdoorsnede onderzoek, hebben we de voedingstoestand van COPD patiënten vastgesteld door middel van de BMI en de MNA (>65 jaar). Van alle 277 patiënten had 6,5% een BMI<18,5 kg/m² en 11,2% een BMI≤21 kg/m². Volgens de MNA hadden drie (2,2%) van de 158 ouderen een slechte voedingstoestand en 23 (16,5%) risico hierop. Daarnaast hebben we gekeken of bepaalde voorspellende factoren voorhanden waren voor (risico op) een slechte voedingstoestand, en of een slechte voedingstoestand geassocieerd was met COPD ernst, dan wel ouderdom. Hoewel dit laatste niet het geval was, werd wel een dalende trend zichtbaar in de gemiddelde BMI bij een toenemende COPD ernst (Global Initiative for Chronic Obstructive Lung Disease (GOLD) stadium 1 t/m 4). Voorspellende factoren waren moeite met het eten van de maaltijd (te moe, klachten tijdens het eten), roken en het gebruik van drinkvoeding. Stoppen met roken en maaltijd instructies, of aanpassingen, zouden interventie mogelijkheden kunnen vormen in de praktijk.

DEEL 2 (Gezondheids) effecten van obesitas en consequenties voor de dagelijkse praktijk

Paragraaf 5.1 beschrijft een verminderde geforceerde expiratoire vitale capaciteit (FVC) en hogere mate van ervaren benauwdheid in obese COPD patiënten. Aangezien dit het hoofdcriterium voor het stellen van de diagnose COPD verhoogd (namelijk de post-bronchodilatatoire expiratoire secondevolume (FEV1)/FVC<0,70), worden obese patiënten waarschijnlijk vaker ondergediagnosticeerd.

Het effect van obesitas op de tien meest voorkomende alledaagse klachten tijdens het spreekuurbezoek wordt beschreven in hoofdstuk 6. In deze studie presenteerden de 550 obese patiënten meer alledaagse klachten aan de huisarts dan de 954 gematchte patiënten zonder overgewicht of obesitas gedurende vijf jaar (incidence rate ratio 1,28; 95% betrouwbaarheids interval 1,12-1,47). Dit betrof de alledaagse klachten: verkoudheid zonder koorts, myalgie van de bovenste gordel, mycosen en contusie/heamatoom, onafhankelijk van de aanwezigheid van chronische ziekten. Deze werkbelasting komt bovenop het spreekuurbezoek voor obesitas gerelateerde chronische comorbiditeit. In de toekomst zal de belasting van de eerste lijn hierdoor verder toenemen.

Paragraaf 6.1 is een brief die de mogelijke rol van de huisarts beschrijft in de huidige obesitas epidemie.

De conclusies van alle studies worden bediscussieerd in hoofdstuk 7, met de rol die de huisarts kan vervullen om een verslechterende voedingstoestand en overgewicht/obesitas te helpen voorkomen. Voor de huisartsen met interesse in voeding is een bredere preventie visie geschetst, met name

taakuitbreiding binnen de gemeenschap. Ook hebben we een aantal ontwikkelingen beschreven, waar de huisarts in de toekomst profijt van kan hebben.



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Dankwoord

Bij de uitreiking van het getuigschrift wist prof. *Chris van Weel* me te interesseren voor de combinatie van de huisartsenopleiding met wetenschappelijk onderzoek, het zogenaamde AIOTHO (Arts In Opleiding Tot Huisarts Onderzoeker) traject. Hierdoor kwam het een paar maanden later tot een ontmoeting met mijn promotor prof. *Jaap van Binsbergen*, huisarts te Brielle, die me sindsdien fascineert met zijn hypothesen en visie op het vak. Beste *Jaap*, ik ben je uiterst dankbaar voor de gedegen en prettige begeleiding. Je combinatie van geduld en humor is goud waard! Ook bood je ondersteuning in 'stormachtige' tijden. Het kompas is eenmaal op hol geslagen; jij, *Toine Lagro* en *Carel Bakx* waren het baken om de koers te hervatten. De hieronder genoemde personen verlichtte deze vaart met meegaande windkracht.

De andere promotores begeleiden veelal op grotere afstand. *Chris*, mijn bewondering voor de altijd snelle en waardevolle redactionele en inhoudelijke correcties van de manuscripten. Door de vele verre reizen heeft dit proefschrift de wereld al gezien. Prof. *Wija van Staveren* was onmisbaar in het geheel. *Wija*, keer op keer scherpte je het geheel aan, of het nu voedingskundig was of niet. Het was speciaal dat je versterking bleef na je eervolle afscheid van de afdeling humane voeding van de Wageningen universiteit in 2004.

Naast de promotores zijn (co-) auteurs belangrijk voor de wetenschappelijke en inhoudelijke vormgeving van het proefschrift. De goede samenwerking bleef niet alleen binnen de afdeling (*Floris van de Laar*, *Erik Bischoff*, *Lisette van den Bemt*, *Tjard Schermer*, *Hans Bor* en *Carel*) of binnen de Radboud universiteit (*Ellen Rasmussen-Conrad*, *Manon van den Berg*, *Thijs Merckx* en *Richard Dekhuijzen*), maar ook andere universiteiten in den lande droegen hun steentje bij (*Margot de Waal*, *Inge Okkes*, *Marjan van den Akker*, *Willem Jan van der Veen* en *François Schellevis* en *Marieke Verheijden*). *Marieke*, ons 'olijfolie ijs' avontuur kan me nog steeds vrolijk maken.

Op de afdeling zijn het de (ex-) collegae AIOTHO's die de wetenschappelijke kracht en geestige noot verder opvoeren, waaronder *Annemarie*, *Erik*, *Evelien*, *Floris*, 'Hiske', *Mark*, *Patrick*, *Raymond*, *Tim* en *Wouter*. *Lotte van den Nieuwenhof* en *Lieke Franke*: jullie gezelligheid en steun heb ik als meer dan collegiaal ervaren in de niet altijd vanzelfsprekende combinatie van onderzoek en praktijk. *Lotte*, ik ben trots op jouw behaalde resultaat! Samen met *Lisette* en *Lotte* waren de laatste loodjes goed te volbrengen. Naast *Chris* en *Tjard*, is *Peter Lucassen* ook altijd begaan geweest met het AIOTHO-schap.

Zoals uit het voorgaande afgeleid kan worden, gaat voedingsonderzoek alleen gepaard met de juiste ambiance. Ondanks dat thee haast niet te slijten was aan mijn kamergenoten, waaronder *Wim de Grauw*, *Erwin Klein Woolthuis*, *Marianne Dees* en *Floris*, was het altijd genieten met de leuke afleidende (achtergrond) gesprekken en de kun-je-even-helpen mentaliteit. *Floris*, je bent een echte kameleon: de ene keer een 'serieuze (computer) hulp', de andere keer een 'ware cabaretier'. Gelukkig was de echte thee liefhebber in het secretariaat gevestigd; *Caroline Roos*, een pauze met jou is een garantie tot ontspanning, evenals de uitjes buiten het werk om! Ook *Margriet Straver*, *Dorothé Jackson* en *Anneke Meijsen* zorgden voor een prettige werksfeer.

Voeding is één onderdeel van een gezonde levensstijl, evenals bewegen. *Reinier Akkermans* en *Hans*, met beide wielrennen als grote hobby, vrolijkten de dag zo nu en dan op met gesprekken over nieuwe fietsen, routes en avonturen. Het bleef niet bij praatjes, zo ondernamen we samen met *Carel* enkele fietstochten. *Hans* fungeerde daarnaast als statistisch klankbord. Ook anderen, binnen en buiten de afdeling, zorgden voor (sportieve) verzetjes met gezelligheid: *Sander Leeuwenburgh*, *Lieke*,

Saskia Zandstra, Marianne, Jente Lange, Evelien Termeer, Natale Adamo en een aantal assistenten van huisartsenpraktijk 'De Linie', maar ook de leden van de *triathlon vereniging Cerberus*.

Onderzoek is praktisch onmogelijk zonder onderzoeksassistenten. *Nicol Orbon* en *Riet Cretier* zetten zich in voor het Monitoring Chronic Obstructive Pulmonary Disease (MONC) project, beschreven in hoofdstuk 5. De weegschaal voor huisbezoeken werd regelmatig in een vrolijke sfeer getest. Ondanks de vele fantasieën, was het onderzoeksbudget helaas te klein om een projectreis te ondernemen met de koffer waarin deze weegschaal vervoerd werd. *Twanny Jeijnsman-Rouwhorst* was mijn steun en toeverlaat bij het aanschrijven van de patiënten en huisartsen uit hoofdstuk 4. *Twanny*, je was mijn reddende logistieke engel in dit project!

De toenmalige stagiaires *Marieke Lemiengre, Annelene van Reenen-Schimmel, Saskia Tabak, Naomi Tillemans* leverden een bijdrage aan dit boekje. *Marieke*, het lijkt me gezellig om nogmaals samen naar het buitenland af te reizen voor een congres. *Florence* was subliem!

In een AIOTHO-traject is ondersteuning vanuit de huisartsenopleiding onontbeerlijk. *Caroline Visser* spande zich keer op keer in om parttime plaatsen te regelen. *Raymond Nypels*, 1^e jaars opleider, heeft me geleerd huisarts te zijn en in zijn praktijk te Gennep bleek hoe waardevol collegae kunnen zijn in het delen van casuïstiek. *Marleen van Casteren*, verpleeghuisarts in hospice Betlehem te Nijmegen, en *Mark Ritzen*, psychiater GGz Nijmegen, hebben me gespecialiseerde kennis bijgebracht. *Thijs Volkers* kreeg te maken met mijn ontwikkelende afgrenzende vermogens, en toonde geduld en begrip, maar vooral interesse.

Een wetenschappelijke huisarts te Doesburg, *Carel*, bracht me binnen in huisartsenpraktijk 'De Linie': het bewijs van de kruisbestuiving tussen wetenschap en dagelijkse praktijk. *Carel*, je motto is patiëntenbetrokkenheid met kwaliteitswaarborg. Hier hoop ik in toenemende mate in bij te dragen. Zonder begrip van *Wilma van Wijk* (praktijkmanager), alle huisartsen (*Erik Gelpke, Natale* en *Virgine Gulikers*, mede dankzij *Carien Klok*) en de assistenten, zou de eindsprint voor dit proefschrift niet mogelijk zijn geweest. Dit laatste geldt zeker ook voor huisartsenpraktijk 'De Schakel' in persoon van *Marianne* (mede dankzij *Rosa Ferwerda*), jullie samenwerking en begrip waren uiterst ademgevend. De praktijk van *Carel* en *Erik* is één van de hoekstenen van de *Continue Morbiditeits Registratie*, welke een grote inhoudelijke bijdrage leverde aan dit boekje (hoofdstuk 3 en 6). Dit registratie netwerk wens ik een warm hart toe; het is zeer waardevol voor talloze zinvolle promotietrajecten!

Ook andere vrienden hebben gezorgd voor de broodnodige ontspanning. Die momenten kenmerkten zich door: humor en relativiteit bij *Krista Saalmink*, interesse en gezelligheid bij *Annemiek Braam*, avontuur en idealisme bij *Artine Anker-de Kool*, sportiviteit en ambitie bij *Jente*, zo nu en dan, maar altijd gezellig met *Luc Walschot* (www.succes.nl), sportiviteit en levensgenot bij *Sander*, rusteloosheid en integriteit bij *René Tijssen*, bescheidenheid en stabiliteit bij *Annechien Langewouters*, warmte en gastvrijheid bij *Ka Wai Wu* (www.succes.nl) en *Judith Visser*, (ex-) liefde en multicultuur bij *Levent Kara*, kracht en doorzettingsvermogen bij *Veronique Mujanovic-Vreeswijk*.

De grafische vormgeving van het proefschrift kwam tot stand via het 'finishing touch' team van *Sander. Jan Leeuwenburgh*: de kaft spreekt boekdelen, maar zonder *Martijn Prins* was het nooit een 'echt' boek geworden!

Hinke Kruizenga, Anja Evers, Janneke Schilp en *Ellen van der Heijden* uit de Stuurgroep ondervoeding, veel succes met het project 'Vroege herkenning en behandeling van ondervoeding in eerstelijnszorg

en thuiszorg’.

Succes is niet te behalen zonder zo’n perfecte achterban. Mijn familieleden zijn zeer eervolle hekkensluiters, net als één van de belangrijkste auteurs in een artikel. Ouders (*Bart* en *Marij*), zus en (schoon) broer (*Aukje* en *Emiel*), jullie geven me heel veel liefde en mentale doorzettingskracht! Vaak werd lachend gezegd dat het onderzoek geen werk was, maar een hobby. *Pappa*, je leverde zelfs een bijdrage door het logo voor het MONC-project in de computer te perfectioneren. Niet te vergeten zorgden mijn nichtjes voor de plezierige afleiding (*Julia*, *Jasmijn*, *Anna* en *Sofie*). Lieve *Katja*, *Seppo*, *opa* en *oma*, ik vind het fijn dat jullie erbij zijn. Heel veel knuffels vanaf papier.



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Curriculum vitae

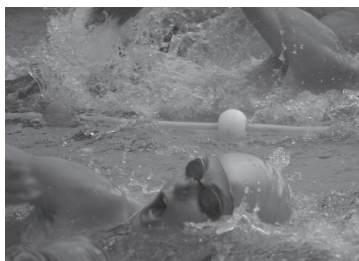
Caroline van Wayenburg werd geboren op 1 maart 1976 in het Universitair Medisch Centrum St Radboud te Nijmegen. Nadat zij de basisschool (De Uilenbrink te Veghel, De Empel te Erp en Stefanus school te Tiel) had afgerond, is zij naar het Atheneum gegaan (R.S.G. Lingecollege te Tiel).

De numerus fixus verhinderde gedurende drie jaar het begin van de studie Geneeskunde. Tijdens de studie Biomedische Gezondheidwetenschappen, gestart in 1994, werd in het kader van haar afstudeerrichting epidemiologie een stage van drie maanden verricht in Finland (Tampere University Hospital bij dr. Terho Lehtimäki) naar genetische factoren (apo E) die het atherosclerotische proces zouden bevorderen. Vervolgens vond een stage van een half jaar plaats op het Julius Centrum te Utrecht, begeleid door dr. Petra Peeters. Waarbij een databestand geanalyseerd werd naar de invloed van de menopauzeleeftijd en de Body Mass Index op het sterfterisico van darmkanker.

In 1998 begon de Geneeskundestudie in een verkort doorstroom programma. Het keuze co-schap werd volbracht op de afdeling gynaecologie in het Akdeniz University Hospital in Antalya, Turkije, bij dokter Eylem Şeker-Ari. Na het behalen van het artsexamen in 2002 ving een enkele maanden durend assistentschap gynaecologie in het Rijnstate Ziekenhuis te Arnhem aan.

De wetenschap bleef evenwel naast patiëntenzorg boeien. In 2003 begon de huisartsopleiding in combinatie met onderzoek, het zogeheten: Arts In Opleiding Tot Huisarts Onderzoeker (AIOTHO) traject. In deze periode werd naast de opleidingsstages, het promotie onderzoek verricht. De opleiding tot huisarts werd in 2008 voltooid. Momenteel werkt Caroline in huisartsenpraktijk 'De Linie' te Doesburg.

Sporten is gedurende de hele studiekeperiode een belangrijke uitlaatklep geweest, als behoud van een optimale energie balans; een voorwaarde voor het verrichten van geestelijke en lichamelijke inspanning. Lang leve de triathlon!



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Illustrations: Jan Leeuwenburgh

Layout: Martijn Prins

