Reports on tasks for scientific cooperation

Report of experts participating in Task 7.3

September 2002

Collection of data on products intended for use in very-low-calorie-diets

Directorate-General Health and Consumer Protection

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Foreword

Scientific Co-operation on Questions Relating to Food
The scope and limitations of this report

Commission Directive 93/5/EC "on the assistance to the Commission and co-operation by the Member States in the scientific examination of questions relating to food" was adopted on 25 February 1993. It lays down a procedure whereby Member States of the European Union can focus their scientific resources in a co-ordinated manner on problems facing the Commission in the area of food. The individual tasks to be undertaken are agreed in consultation with the Member States who also determine in which tasks they wish to participate and the extent of their participation. Directive 93/5/EC requires that an inventory of tasks is published at least every six months. This publication, which takes the form of a Commission Decision, specifies the participating Member States, the Member State which provides co-ordination and the time limit for completion of the task.

In general terms, tasks undertaken under scientific co-operation are designed to provide a factual basis to support a Commission action in the area of food. Such support may involve the provision of information as may be required, for example, by the Scientific Committee on Food (SCF) for its evaluation and advisory work or by the Commission's own services for the development of proposals for Community Action.

The tasks themselves are carried out by a group of experts nominated by the National Authorities responsible for Scientific Co-operation in the Member States (the National Designated Authorities).

Although the scope of reports generated under the scientific co-operation procedure is restricted to essentially factual matters, presentation of inherently complex information without some reasoned interpretation and summary by specialists would be of limited value and even open to misleading conclusions. Such interpretation necessarily involves a degree of expert judgement.

It is therefore stressed that the interpretation and views expressed in this report are not necessarily those of the participating Member States or those of the European Commission.

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EXECUTIVE SUMMARY

This report is the result of the work undertaken within task n° SCOOP 7.3 "Collection of data on products intended for use in very low calorie diets" established under Directive 93/5/EC on the assistance to the Commission and Co-operation by the Member States in the Scientific Examination of Questions related to food. This task was co-ordinated by The Netherlands in collaboration with Belgium, Denmark, Finland, France, Germany, Ireland, Italy, Portugal, Sweden, the United Kingdom and Norway as non-EU country.

The terms of reference were to collect information on:

A. Current legislative situation on VLCDs in the participating Member States;
B. Inventory of existing products already on the market;
C. Review of the scientific literature about safety and efficacy leading to indications and contra indications for the use of VLCDs;
D. Advice on the information that should be conveyed to the consumer of VLCDs;
E. Recommendation for further research.

For this task the working group agreed to use a number of scientific reviews about the topic of obesity and VLCDs as basic information for the preparation of the report as well as the Codex standard regulation (CODEX STAN 203-1995) as working document.
The following working definition of VLCD was accepted: *"Very low calorie diets are formulated food with an energy content between approximately 450 and 800 kilocalories daily. These foods are intended for use, as presented, except for the addition of water where applicable, as the sole dietary source of energy and all essential nutrients required in excess weight loss programmes."*

The minimal energy level of approximately 450 kcal is in line with the CODEX standard regulation. In this report results from VLCDs with lower energy intake levels will be used in some paragraphs to illustrate the topic in the perspective of a larger energy intake range as well as the existing VLCD product availability in the EU.

A. CURRENT LEGISLATIVE SITUATION ON VLCDs IN THE PARTICIPATING MEMBER STATES

The regulatory framework for VLCDs within the EU has been reviewed.

- Directive 89/398/EC, foodstuffs intended for particular nutritional uses. Sofar specific legislation for certain type of slimming foods has been adopted as Commission Directive 96/8/EC. However, the scope of this legislation is limited to compositional, labelling and advertising controls for food presented as "total diet" or "meal replacement". The energy content of the total diet is specified as between 800 and 1200 kcal. Total diets below 800 kcal c.q. VLCD fall outside the scope of the Directive

and specific rules for this category of daily diet replacement shall be adopted at a later stage. The activities within this SCOOP task 7.3. focus on the collection of information necessary to prepare these specific rules.

- Other relevant directives, relevant to VLCDs are Commission Directive 2000/13/EC on labelling, presentation and advertising of foodstuffs, Commission Directive on nutrition labelling for foodstuffs (90/496/EC), food additives authorised for use in foodstuffs intended for human nutrition (89/107/EC) and Commission Directive (99/21/EC) on dietary foods for special medical purposes as well the non-statutory international Codex Standards on the labelling and claims of VLCD (CODEX STAN 146-1985) and on Formula Foods for use in Very Low Energy Diets for weight reduction (CODEX STAN 203-1995).

B. INVENTORY OF EXISTING PRODUCTS ALREADY ON THE MARKET

- Based on the inventory of existing regulation availability can be classified in four categories:
  - Restricted use under medical supervision and restricted availability in hospitals (DE)
  - Available on prescription only (FR)
  - Available in pharmacy only (BE)
  - Freely available (DK, FI, IE, IT, NL, NO, PT, SE, UK)

  All countries have rules about declaration of nutrient content, when and how to use and advice about contra-indications and exclusion of population groups at risk such as infants, children or pregnant women.

- 14 Different VLCDs from different companies have been identified and characterized on basic information such as type and dosage, preparation, variants, availability, costs, energy and nutrient content as well as labelling information on the package about contra-indications, treatment duration, user instructions, marketing, claims as well as additional scientific documentation. The estimated sales volume in the EU ranged between 110,000 and 65,000 person months of use between 1995 and 2000.

C. REVIEW OF THE SCIENTIFIC LITERATURE ABOUT SAFETY AND EFFICACY LEADING TO INDICATIONS AND CONTRA-INDICATIONS FOR THE USE OF VLCDs

- Obesity is one of the most rapidly increasing health concerns in the EU as well as globally. Prevalence data from the different European countries indicate that 30 to 50 % of the adult population can be considered as overweight (BMI[1] > 25 kg/m^2) and 10 to 30 % as obese (BMI > 30 kg/m^2). Also the prevalence of obesity among children and adolescents is rapidly increasing. With increasing BMI health risks are increased.

Especially with a BMI over 30 risks of co-morbidities and mortality increases exponentially. Risk of type II diabetes, gall bladder disease, dyslipidaemia and sleep apnoea is greatly increased (> 3 times) while risk of cardio-vascular disease, hyper-

[1] BMI = Body Mass Index = body weight (kg)/height^2 (m)

tension, osteoartritis and gout is moderately increased (2-3 times). Therefore the directly related health care cost of obesity is estimated between 2 and 6 % of total health care expenditure. Even a moderate degree of weight loss (5 % BW) has been shown to reduce health risks.

- So far dietary treatment is considered to be the cornerstone of weight loss programmes. The basic element is energy restriction. In theory VLCD will lead to greater weight losses compared to LCD although most randomized controlled trials did not show these differences, most probably due to differences in compliance. Based on the existing literature it is suggested that an initial greater weight loss improves long-term weight maintenance, providing that it is followed by supported integrated weight management programmes.

- Relative to the energy deficit the human body will change metabolism in order to adapt to the relative energy shortage. Resting Metabolic Rate is decreased, partly related to the reduction in Fat Free Mass (FFM) and partly due to a reduction of energy metabolism per unit of FFM. The latter will be restored during refeeding. Several hormonal changes and substrate alterations occur during energy restriction involving cathecholamines, thyroid hormones, insulin, glucagon, growth hormone and leptin.

- As a consequence of the metabolic adaptation there is an increasing risk of loss of excessive body protein. The working group considered that VLCDs containing a minimum of 50 g protein per day with a minimum of 55 g/day available carbohydrate would spare body protein. Enhancement of ketogenesis will also increase protein sparing. This enhancement in ketogenesis is negatively related to the level of carbohydrate intake. Therefore both the direct protein sparing effect of addition of carbohydrate as well as the non-ketogenic property of higher levels of carbohydrate should be taken into consideration to advise on optimal daily level of protein and carbohydrates. It is the opinion of the working group that this is at a level of about 50 to 60 g available carbohydrate per day. Energy restriction and ketosis will lead to a negative calcium balance and increased blood concentration of uric acid. Both are not directly related to VLCD but more to hypoenergetic diets in general. Increase in the calcium levels of VLCDs and exclusion of potential users of VLCDs with a recorded history of gout will prevent these side effects.

- For the determination of safety and efficacy over 460 studies covering 52,000 dieters have been reviewed. A number of minor side effects are reported including dry mouth, obstipation/diarrhoea, headache, dizziness, nausea, cramps, fatigue, hunger, feeling cold and hair thinning. Most are temporary and avoidable with appropriate measures. More severe occasionally reported adverse events most probably related to VLCD are acute gout, cholelithiasis and acute psychosis. Other reported adverse events most probably not related to VLCD are foot drop, diabetic ketoacidosis and cardiac arrhythmias. Cholelithiasis is considered not to be an extra risk if the minimum fat content of the VLCD is 7 g per day.

- An extensive analysis of the literature of the risk of using VLCD with a BMI between 25 and 30 kg/m^2 compared to over 30 did not reveal any extra loss of FFM vs. FM as was claimed in the past. Analysis of the weight loss FFM/FM ratio as a function of energy level of the VLCD (400-600, 600-800 and 800-1200 kcal) did not reveal any relationship.

- Based on the existing literature on safety and efficacy of the use of VLCD as well as the existing Codex Standard regulation the working group used the following list of components and quality factors for their safety review.
  - Protein: 50 g or more with a PDCAAS (Protein Digestibiliy-Corrected Amino Acid Score) of 1
  - Fat: 7 g or more with a minimal intake of linoleic and alpha-linolenic acid of resp. 3.0 and 0.5 g
  - Carbohydrate: 55 g or more of available carbohydrates
  - Fiber: 10 g or more fiber of defined type
  - Vitamins and minerals: similar values as stated in Commission Directive 96/8/EC with Manganese (1 mg) and Chromium (33 μg).

D. ADVICE ON THE INFORMATION THAT SHOULD BE CONVEYED TO THE CONSUMER OF VLCDs

The working group has extensively discussed aspects directly related to the consumer and came to the following conclusions.

Availability

In all countries except one, VLCDs are available at the retail level. The working group concluded that there is no evidence of any problems.

Advice for consumers

The information, including nutrition labelling, made available on the package has been reviewed.

Suggested description of the product:

- "Slimming product with very low energy content for the dietary management of excess weight"
- Suggested there should be full nutrional labelling
- Contra-indications which can be divided into three categories:
  * Persons for whom VLCDs are unsuitable;
  * Diseases or conditions where VLCDs are absolutely contra-indicated or where additional supervision and/or changes to treatment regimens may be required;
  * Other information or conditions for an effective and safe use of VLCDs.
- Other information on the package such as advice on:
  * Consumption of adequate amounts of water;
  * Consultation of a physician in case of medical treatment or medical history;
  * Period of use without medical consultation.

Claims

Legislative controls or voluntary agreements on claims on products were reviewed.

E. RECOMMENDATION FOR FURTHER RESEARCH

- The working group noticed the lack of information about the profile of the VLCD consumer. It recommends further research on this topic in order to be more specific in the regulation of the required information for the user.

CHAPTER 1

Task 7.3 SCOOP-VLCD

1.1. Background

Energy restricted diets below 800 kilocalories daily, also called very low calorie diets (VLCDs), are not regulated by the Commission Directive 96/8/EC "Food intended for weight control". These VLCD products have already been on the market in some EU countries for several years. In the Commission Directive 96/8/EC it is stated that "specific rules for these very low energy products will be adopted at a later date".
Under the Commission Directive 93/5/EC article 1 regarding the assistance to the Commission and co-operation by the Member States in the scientific examination of questions related to food (SCOOP), The Netherlands have requested the task "Collection of data on products intended for use in very low calorie diets" in collaboration with Belgium, Denmark, Finland, France, Germany, Ireland, Italy, Portugal, Sweden, United Kingdom and Norway. The latter as non-EU country.

1.2. Overall objectives

The main objective of the task is to prepare a report that summarizes the existing knowledge of VLCDs with regard to:

- Current legislative situation in the participating Member States on VLCDs;
- An overview of the form and composition of existing products already on the market in the participating Member States;
- The indications and contra-indications for the use of VLCDs in relation to their composition based on a review of the existing scientific literature about the safety and efficacy of VLCDs;
- Advice on the special information that should be conveyed to the consumer of VLCDs;
- Recommendation for further research.

1.3. The approach used in this task

During the first plenary meeting in Maastricht, The Netherlands, held on March 15th and 16th 2000, the working group agreed to develop their work in the following way.

a) Since **the theme of obesity and the use of VLCDs** have extensively been reviewed from a scientific point of view over the past two decades, it was decided to use these documents as basic information for the preparation of the report. In addition to this, it was decided to summarize only general information about obesity and the use of VLCDs in the report and to refer to the existing scientific literature for more detailed information (see Section 1.4 - Consulted documents).

b) **Current legislative situation in the participating Member States on the use of VLCDs.** Participants agreed to prepare a general questionnaire and, based on this questionnaire, to collect the necessary information from the different authorities within each country. Such an assessment may form part of the information used to advise on the legislative aspects of VLCDs within the European Union.

c) **To collect data on form and composition of existing products already available on the market in the participating Member States.** The VLCD Industry Group made an inventory about this issue and the report was accepted as valuable input for answering this question of Task 7.3 of SCOOP. Furthermore, based on a standardized protocol, each participant collected the information that is relevant for each country. It was recognized that it is difficult to have a complete overview of the market as it is a very dynamic one where products come and go.

d) SCOOP activities are normally undertaken to provide factual information from the various participating Member States. The terms of references related to **indications and contra-indications for the use of VLCDs in relation to their composition,** demand a review of the existing scientific literature about safety and efficacy of VLCDs. The participants agreed the fact that this task includes interpretation of existing data and the acceptance of a composition of the products as well as a set of criteria for the use of VLCDs to be used as the basis of the working group's safety evalution. Consensus was reached that a number of reviews, published in the past, would serve as a basis for the report (see Section 1.4 - Consulted documents).

Based on a MedLine search recent publications were identified, discussed and added to the database of literature upon which the report is written.

e) As a final task the working group prepared and discussed a chapter on **the advice on special information that should be conveyed to the consumer of VLCDs.**

f) It was agreed to use the **Codex Standard** (CODEX STAN 203-1995) as a working document and to collect information and discuss the issues along the lines of this regulation.

1.4. Consulted documents

Over the years many reports and reviews have been published in the area of VLCDs and obesity. Therefore, it was concluded at the start of this Task that a number of issues should only be discussed briefly in the report. The following reports and reviews were examined in depth and were considered as valuable documents in relation to this SCOOP Task.

- WHO Consultation, 1998
  Obesity, preventing and managing the global epidemic.
  Report of a WHO Consultation on Obesity. Geneva, June 1997.
  WHO Publications: Geneva.

- AACE / ACE Obesity Task Force, 1998
  Position statement on the prevention, diagnosis and treatment of obesity.
  www.aace.com/clin/guides/obesity.

- Nordic Council of Ministers, 1994
  Dietetic Foods. Proposed Nordic Guidelines for assessment and regulation.
  Tema Nord 1994: 580.

- Health Council of the Netherlands. Joint Committee of the Health Council and the Nutrition Council. Advice on very low calorie diets.
  Report No 1986/3, The Hague, 1986 (in Dutch).

- COMA. Committee on Medical Aspects of Food Policy.
  The Use of Very Low Calorie Diets in Obesity.
  Report on Health and Social Subjects No. 31, HMSO, London, 1987.

- National Task Force on the Prevention and Treatment Of Obesity, 1993
  Very low-calorie diets.
  JAMA 270: 967-974.

- VLCD European Industry Group, 1998
  Report to the SCOOP Committee on very low calorie diets (VLCD).

- VLCD European Industry Group, 2000
  Very low calorie diets. Information on products currently available in Europe.
  VLCD Industry Group Report, July 4th 2000.

- Marks J, Schrijver J, 2001
  Reports submitted on behalf of the VLCD European Industry Group to the SCOOP working group on very-low-calorie diets between 1998 and 2001 consolidated, 2001.
  www. Foodedsoc.org/VLCD

- CODEX STAN 203-1995
  Standard for formula foods for use in very low energy diets for weight reduction.
  www.codexalimentarius.net/STANDARD/volume 4/vol4_E.htm

- CODEX STAN 180-1991
  Codex Standard for the labelling of and claims for Foods for Special Medical Purposes.
  www.codexalimentarius.net/STANDARD/volume 4/vol4_E.htm

CHAPTER 2

Definition of terms by Codex in relation to this SCOOP activity

2.1. Background

Energy restricted diets below 800 kilocalories daily, also called very low calorie diets (VLCDs) or very low energy diets (VLEDs), are not regulated by the Commission Directive 96/8/EC of 26 February 1996 on foods intended for use in energy-restricted diets for weight reduction. In this Directive, it is stated that "specific rules for these very low energy products will be adopted at a later date". These VLCD products have already been on the market for several years. However, legislation concerning the definition, composition, labelling, directions of use and the availability of such products on the market varies considerably across Europe. The principle of free trade within the EU implies free movement of foodstuffs from one country to another, unless there is a public health concern preventing this. The working group of SCOOP Task 7.3 has the opinion that specific regulation could be developed for this category of food for particular nutritional uses (PARNUTS). It was agreed to adapt in general the existing Codex Alimentarius Standard Regulations for Formula Foods for use in Very Low Energy Diets for Weight Reduction (CODEX STAN 203-1995).

2.2. Codex definitions

A proposal for a draft Codex standard for VLCD including a definition was prepared by the delegation of the Netherlands in 1991 (CX/NFSDU 91/11). Originally they were defined as follows: *"A formula food for use in very low calorie diet is a food specially prepared to supply a minimum amount of carbohydrates and the daily requirements of the essential nutrients in 450-600 calories which represents the sole source of energy intake*". A minimum content of 50 g of carbohydrates and 50 g of protein, respectively, were also recommended in the first proposal. To avoid a gap between 600 and 800 kilocalories in relation to the Codex Standard for Formula Foods for Use in Weight Control Diets (CODEX STAN 180-1991), the final Codex definition applies to all formula foods for weight reduction supplying less than 800 kilocalories per day. The term 'calorie' in reference to the diet was replaced by 'energy' in the title of the draft standard and throughout the document. Because of health risks associated with very low calorie diets (VLCDs), especially in the early days with inferior ingredients, it was also accepted that within the scope includes the definition, "*These foods are defined as foods for special medical*

purposes and must be used under medical supervision by individuals with moderate or severe obesity" in view of the need for patient selection and medical management during the diet period and the re-feeding stage. Frequently the patients have obesity-related complications such as hypertension or diabetes that require careful monitoring (cf. CX/NFSDU 92/5-Add.2).

2.3. SCOOP definitions

In the working group the different aspects of the definitions were discussed.

2.3.a. VLCD versus VLED

From the theoretical point of view, the term 'energy' in the definition is preferred. Furthermore, in relation to the System International (S.I.) the term 'calorie' is not acceptable anymore. However, over the years the term 'very low calorie diet (VLCD)' is generally accepted and is nowadays used for formula diets intended to be used for weight reduction. Therefore the working group accepted the term 'VLCD' as working definition for this category of formula food.

2.3.b. Obesity, overweight and excess weight

The following BMI cut-off points for the different weight related terms were accepted:

- underweight BMI < 18.5 kg/m^2
- normal weight BMI 18.5 – 24.9 kg/m^2
- overweight BMI 25.0 – 29.9 kg/m^2
- obesity BMI ≥ 30.0 kg/m^2
- excess weight BMI ≥ 25.0 kg/m^2

2.3.c. Energy range of VLCDs

Also the range of energy intake levels per day was subject to an intense debate within the working group. In the existing regulation by the Commission Directive 96/8/EC rules have been set for foods intended for use in energy restricted diets from 800 kilocalories and higher. Therefore, the upper limit for VLCDs is 800 kilocalories. In the Codex a minimal content of 450 kilocalories as the only source of energy is given. Although the minimal energy content depends on the minimal standards for the macronutrients, protein, carbohydrates and fats, the working group accepted the Codex Standard of 450 kilocalories as minimal energy level of the VLCD food as only source of energy.

It was decided not to review scientific data based on VLCDs with a lower level than 400 kilocalories per day as only energy source. Only in the case of comparison of different levels of energy intake on metabolic functions and safety studies below the 400 kilocalories level will be quoted.

2.3.d. Working definition of VLCD

Finally, the Codex definition of VLCD was discussed and simplified as follows:

"Very low calorie diets are formulated foods with an energy content between approximately 450 and 800 kilocalories daily. These foods are intended for use, as presented, except for the addition of water where applicable, as the sole dietary source of energy and all essential nutrients required in excess weight loss programmes".

CHAPTER 3

Regulatory framework for very low calorie diets within the EU

3.1. Commission Directive 89/398/EC

Foodstuffs intended for particular nutritional uses (**PARNUTS**)

Harmonised Community rules for *foodstuffs intended for particular nutritional uses (parnuts)* are laid down in Commission Directive 89/398/EC as amended by Directive 1999/41/EC. Article 1(2)(a) of this framework Directive defines parnuts foods as:
"foodstuffs which, owing to their special composition or manufacturing process, are clearly distinguishable from foodstuffs for normal consumption, which are suitable for their claimed nutritional purposes and which are marketed in such a way as to indicate such suitability".

Foodstuffs for particular nutritional uses are required to fulfil the particular nutritional requirements of certain categories of persons:

- *whose digestive processes or metabolism are disturbed; or*
- *who are in a special physiological condition and who are therefore able to obtain special benefit from controlled consumption of certain substances in foodstuffs; or*
- *infants or young children in good health".*

The Annex to the Directive lists those groups of foods for which specific legislation shall be adopted and includes food intended for use in energy-restricted diets for weight reduction. The remaining categories are:

- infant formulae and follow on formulae;
- processed cereal-based foods and baby foods for infants and young children;
- dietary foods for special medical purposes;
- foods intended to meet the expenditure of intense muscular effort, especially for sportsmen.

The Directive also requires the Commission to develop specific rules for the use of certain claims (sodium free, reduced sodium, and gluten-free) and to consult the Scientific Committee on Food (SCF) and present a report to the European Parliament and to the Commission, by 8 July 2002, on the desirability of specific controls on foods for persons suffering from diabetes.

The Directive provides a framework within which the foods listed above, and other parnuts foods that are not subject to specific legislation should be regulated and states the principles for regulation, namely, their characterisation, nature and composition, and labelling. It also provides for parnuts foods to make a claim about their particular suitability for their target population. Article 7 of the Directive requires that *"The designation under which a product is sold shall be accompanied by an indication of its particular nutritional characteristics"*. Further: *"The labelling of products for which no specific Directive has been adopted,* which is currently the case for very low calorie diet (VLCD) products, *must also include:*

- *the particular elements of the qualitative and quantitative composition or the special manufacturing process which gives the product its particular nutritional characteristics;*
- *the available energy value expressed in kilojoules and kilocalories and the carbohydrate, protein and fat content per 100 grams or 100 millilitres of the product as marketed and, where appropriate, per specified quantity of the product as proposed for consumption".*

Specific legislation for certain types of slimming foods has been adopted as Commission Directive 96/8/EC on foods intended for use in energy-restricted diets for weight reduction. The scope of this legislation is limited to compositional, labelling and advertising controls for foods presented as 'total diet' or 'meal' replacements for weight control purposes. The energy content of total diet replacements is specified as between 3,360 kJ (800 kilocalories) and 5,040 kJ (1,200 kilocalories) per day. VLCDs with a lower energy content fall outside the scope of the Directive. However the recitals indicate that specific rules for very low energy products intended to replace the whole of the daily diet shall be adopted at a later date.

3.2. Other Directives relevant to VLCDs

3.2.a. Commission Directive on the approximation of the laws of the Member States relating to the labelling, presentation and advertising of foodstuffs (Commission Directive 2000/13/EC)

The Directive consolidates the provisions of Commission Directive 79/112/EC, adopted in 1978, and subsequent amending Directives. For the purposes of the Directive labelling means (Article 1): *"any words, particulars, trade marks, brand name, pictorial matter or symbol relating to a foodstuff and placed on any packaging, document, notice, label, ring or collar accompanying or referring to such foodstuffs".* The Directive concerns the labelling of foodstuffs delivered as such to the ultimate consumer and certain aspects relating to the presentation and advertising. It also applies to foodstuffs intended for supply to restaurants, hospitals, canteens and other similar mass caterers.

Article 2 prohibits labelling which could mislead consumers and places certain restrictions on claims:

"1. The labelling and methods used must not:

(a) be such as could mislead the purchaser to a material degree, particularly

(i) as to the characteristics of the foodstuffs;

(ii) by attributing to the foodstuff effects or properties which it does not possesses;

(iii) by suggesting that the foodstuff possesses special characteristics, when in fact all similar foodstuffs possess such characteristics;

(b) subject to Community provisions applicable to… foodstuffs for particular nutritional uses, attribute to any foodstuff the property of preventing, treating or curing a human disease, or refer to such properties.

2. The prohibitions and restrictions referred to… shall also apply to:

(a) the presentation of foodstuffs, in particular their shape, appearance or packaging, the packing materials used, the way in which they are arranged and the setting in which they are displayed;

(b) advertising".

The labelling must include: the name of the product; a list of ingredients; the quantity of certain ingredients or categories of ingredients; the net quantity; date of minimum durability; any special storage conditions or conditions of use (Article 3); and the name or business name and address of the manufacturer or packer. The Directive also requires that information about the particulars of the place of origin of the food must be declared if failure to do so would mislead the consumer to a material degree, and instructions for use must be given if it would be impossible to make appropriate use of the food in the absence of such instructions.

The list of ingredients shall include all the ingredients (including additives) of the foodstuff, in descending order of weight and preceded by a suitable heading which includes the word: "ingredients".

The category and specific names and E-numbers of the additives are given in the following Directives (which can be found at the Internet addresses given in brackets):

- Council Directive of 21 December 1989 on the approximation of the laws of the Member States concerning food additives authorized for use in foodstuffs intended for human consumption (89/107/EC). OJ L 40, 11.02.1989, p.27 (http://europa.eu.int/eur-lex/en/consleg/pdf/1989/en_1989L0107_do_001.pdf)
- European Parliament and Commission Directive 94/35/EC of 30 June 1994 on sweeteners for use in foodstuffs. OJ L 237, 10.09.1994, p.3 (http://europa.eu.int/eur-lex/en/consleg/pdf/1994/en_1994L0035_do_001.pdf)
- European Parliament and Commission Directive 94/36/EC of 30 June 1994 on colours for use in foodstuffs. OJ L 237, 11.09.1994, p.13 (http://europa.eu.int/eur-lex/en/consleg/pdf/1994/en_1994L0036_do_001.pdf)

- European Parliament and Commission Directive 95/2/EC of 20 February 1995 on food additives other than colours and sweeteners. OJ L 61, 18.03.1995, p.1 (http://europa.eu.int/eur-lex/en/consleg/pdf/1995/en_1995L0005_do_001.pdf

The labelling of flavourings is indicated in:

- Commission Directive of 22 June 1988 on the approximation of the laws of the Member States relating to flavourings for use in foodstuffs and the source materials for their production (88/388/EC). OJ L 184, 15.07.1988, p.61 (http://europa.eu.int/eur-lex/en/consleg/pdf/1988/en_1988L0388_do_001.pdf)

3.2.b. Commission Directive on nutrition labelling for foodstuffs (90/496/EC)

The nutrition labelling Directive applies to parnuts foods without prejudice to the requirements laid down in Directive 89/398/EC or other specific subsidiary legislation. For foods generally, nutrition labelling may be given voluntarily, but is mandatory if a nutrient claim is made (Article 2). A nutrition claim is defined as (Article 1): *"any representation and any advertising message which states, suggests or implies that a foodstuff has particular nutrition properties with respect to its energy and/or nutrient content".*

When nutrition labelling is given it must be provided in one of two standard formats. The minimum format includes the energy value and the amounts of protein, carbohydrate and fat. The second format includes those nutrients listed above plus information for sugars, saturated fatty acids, fiber and sodium. The nutrition declaration must include information about any nutrient for which a claim is made. Information about the amounts of mono-unsaturated fatty acids, poly-unsaturated fatty acids and cholesterol, vitamins and minerals (Article 4) may also be given.

Where energy is declared it must be given in kilojoules and kilocalories. The amounts of protein, carbohydrate, fat, fiber and sodium must be given in grams, and cholesterol in milligrams. Vitamins and minerals must be declared in accordance with the units (milligrams or micrograms) specified in the Directive. Nutrient information shall be expressed per 100 g or 100 ml, as appropriate, and may in addition be given per serving or per portion. For vitamins and minerals information must also be expressed as a percentage of the relevant recommended daily allowance (RDA)(Article 6) specified in the Directive per 100 g or 100 ml. The percentage RDA of vitamins and minerals per quantified serving, or, per portion of the food provided that only one such portion is contained in the sales unit of the food may be also given voluntarily.
It should be included that the vitamin and mineral declaration in nutrition labelling is allowed only if the level of a vitamin or mineral is at least 15% of the RDA (given in the Annex) per 100 g or 100 ml (or per portion if the packaging consists of only one portion).

3.2.c. Commission Directive on the approximation of the laws of the Member States concerning food additives authorised for use in foodstuffs intended for human nutrition (89/107/EC)

The term food additive is defined in Article 1 of the Directive as: *"any substance not normally consumed as a food in itself and not normally used as a characteristic ingredient of food whether or not it has nutritive value, the intentional addition of which to food for a technological purpose in the manufacture, processing, preparation, treatment, packaging, transport or storage of such food results, or may be reasonably expected to result, in it or its by-products becoming directly or indirectly a component of such foods".* The Directive does not apply to flavourings which fall within the scope of Commission Directive 88/388/EC, or to substances added to foodstuffs as nutrients, such as minerals, trace elements and vitamins. Food additives commonly used in VLCD products include colours, preservatives, anti-oxidants, sweeteners, stabilisers, emulsifiers and thickeners. Specific provisions for some of the above-mentioned additives (apart from flavourings) are laid down in specific Directives.

The Commission has adopted lists of 'authorised' additives and lists of foodstuffs to which these additives may be added. Such lists are included in the respective Directives.

Article 8 requires that the labelling of an additive intended for sale to the ultimate consumer must appear on the packaging as its *"name laid down by any Community provisions applying to the product in question plus its EC number, or, in the absence of such provisions, by a description of the product that is sufficiently precise to enable it to be distinguished from products with which it could be confused".*

3.2.d. Commission Directive on dietary foods for special medical purposes

The European Directive is: Commission Directive 1999/21 EC of 25 March 1999 on dietary foods for special medical purposes. OJ L 91, 7.4.1999, p. 29. The full text can be found on the Internet address:
(http://europa.eu.int/eurlex/en/consleg/pdf/1999/en_1999L0021_do_001.pdf).

3.3. Non-statutory International Standards

Codex Standard on Very Low Calorie Diets

The Codex Alimentarius Commission has adopted an international standard for very low calorie diets, which are categorized as parnuts foods. Codex Alimentarius (CODEX STAN 146-1985) defines these parnuts as follows:
"Foods for special dietary uses are those foods which are specially processed or formulated to satisfy particular dietary requirements which exist because of a particular physical or physiological condition and/or specific diseases and disorders and which are

presented as such. The composition of these foodstuffs must differ significantly from the composition of ordinary foods of comparable nature, if such ordinary foods exist".

Recommendations for the energy, protein, carbohydrate, linoleic and alpha-linolenic acid, and micronutrient content of VLCDs have been adopted by Codex Alimentarius as CODEX STAN 203-1995. The requirements of the standard are not statutorily binding unless implemented into national legislation.

3.4. Regulation attached to VLCDs in European countries

In Table 3.1. the regulations related to VLCDs are listed for a number of countries in Europe. The table was constructed by means of information given by each of the participating countries. The table gives the specific regulation according to implementation of EU-Directives with relevance for VLCDs (column 2), other non-statutory conditions or agreements which countries impose on VLCDs (column 3). Further, the table gives the requirements for nutrient contents of VLCDs (column 4). There exist some differences especially with respect to EFA (Essential Fatty Acid) and fiber. Some countries require premarket approval others do not (column 5). Availability of VLCD products within Europe varies from country to country (column 6). Availability can be classified into the following categories:

- VLCD products that are prescribed for selected patients under medical supervision and which are only available in hospitals or comparable situations. This applies to *Germany.*
- VLCD products which are available on prescription only. This applies to *France.*
- VLCD products which are available in pharmacies only. This applies to *Belgium.*
- VLCD products that are freely available i.e. there are no restrictions. This applies to *Denmark, Finland, Ireland, Italy, The Netherlands, Portugal, Sweden, The United Kingdom, and Norway,.*

Only one country (Denmark) has imposed a regular compositional control on VLCDs apart from that required by the companies according to GMP (column 6).

Table 3.1. Conditions for nutrient contents, approval, availability and compositional control for VLCD-products in Europe

Country	Specific regulation	Non-statutory conditions	Nutrient content	Pre-market approval	Availability	Compositional control
Belgium	Belgian Royal Decrees of 18 Feb 1991 and of 27 Sept 1993 describing the rules for the use of low energy products. European Directive 96/8/EC; related to the use of energy-restricted diets for weight control.	Report of the Scientific Committee for Food of the European Communities on Food Intended for Weight Control (1991).	Yes. Minimum and maximum contents: energy, vitamins and minerals. Minimum contents: protein, carbohydrate and linolenic acid.	Yes. Belgian Food Administration	Pharmacies.	Yes. Only at approval.
Denmark	Governmental order on "Foods for specific dietary purposes" (No 162, 15 March 1991).	Codex Alimentarius Standard: "Standard for Formula Foods for Use in Very Low Calorie Diets". Nordic Nutrient Recommendations.	Yes. Minimum and maximum contents: energy, vitamins and minerals. Minimum contents: protein, carbohydrate, linoleic acid and linolenic acid. Maximum content: fiber.	Yes. Danish Veterinary and Food Directorate.	No restrictions.	Yes. Yearly analytical control of micronutrient content.
Finland	Decision of the Ministry of Trade and Industry on "Foods for specific dietary purposes" (937/95) based on the Food Act (361/95).	TemaNord 1994:580: "Dietetic Foods – Proposed Nordic Guidelines for Assessment and Regulation".	Yes. Minimum and maximum contents: energy, vitamins and minerals. Minimum contents: protein (quantity and quality), carbohydrate, linoleic and linolenic acid.	No.	No restrictions.	No. Only occasional control.
France	Governmental order on "Foodstuffs intended for particular nutritional uses". Governmental order on "Specific Requirements on Substances that may be Added for Specific Nutritional Purposes in Foods for Particular Nutritional Purposes (Aug 4 1986). Governmental order on labelling (articles R.112-1 to R.112-33 from the Consumption Code).	Opinion of the interministerial committee studying products intended for particular nutritional uses (CEDAP), Oct 8 1997, relative to dietary products intended for energy-restricted diets supplying less than 800 kcal per day (compositional requirements).	Yes. Minimum and maximum contents: energy. Minimum contents: protein, carbohydrate, linoleic and linolenic acid, and vitamins and minerals.	No.	On prescription only.	Yes.
Germany	Governmental order on "Foods for Special Dietary Uses" DiätVO, revised version 5th May 1999.	Exception to the use of other than energy restricted diets for weight reduction (>800 kcal) – produced on the advice of the physician.			Can only be used on selected patients under medical supervision in hospitals or in comparable situations.	

Country	Specific regulation	Non-statutory conditions	Nutrient content	Pre-market approval	Availability	Compositional control
Netherlands	Governmental order on "Dietary products intended for energy-restricted diets for weight reduction" (No 683013, Stert, 250 and 254 20 Dec 1988) with amendments (March 10 1997, 971233, Stert, 52; amended March 17, 2000).	None.	Yes. Minimum and maximum contents: energy, vitamins and minerals. Minimum contents: protein, carbohydrate and linoleic acid. Maximum content: fat.	No.	No restrictions.	No.
Norway	Governmental order on "Foods for specific dietary purposes" (No 1382, 21 Dec 1993). "Production and Marketing of Foods" (No 1252, 8 July 1983).	Codex Alimentarius Standard: "Standard for Formula Foods for Use in Very Low Calorie Diets". TemaNord 1994:580: "Dietetic Foods – Proposed Nordic Guidelines for Assessment and Regulation".	Yes. Minimum and maximum contents: energy, vitamins and minerals. Minimum contents: protein, carbohydrate, linoleic acid and linolenic acid. Maximum content: fiber.	Yes. Norwegian Food Control Authority.	No restrictions.	No. Only requested by suspicion or complaints.
Portugal	Decreto-Lei 227/99 de 22 de Junho; transposed EC Directive 89/398/EEC. Additives: Decreto-Lei 363/98, de 19 de Junho; EC Directive 94/35; EC Directive 94/36. Labelling: Decreto-Lei 170/92, de 8 de Agosto, Portaria 119/93, de 2 de Fevereiro and Portaria 751/93, de 23 de Agosto.	Compositional requirements: Codex Alimentarius Standard 203-1995 and Annex of Directive 96/8/EC.	Yes. Minimum and maximum contents: energy, vitamins and minerals. Minimum contents: protein, carbohydrate, linoleic acid and linolenic acid. Maximum content: fiber.	No. Notification only to Directorate-General for Health.	No restrictions.	Yes. If decided by the Directorate-General for Health
Sweden	Governmental order on "Foods for particular nutritional uses" (SLVFS 2000:14).	TemaNord 1994:580: Dietetic Foods - Proposed Nordic Guidelines for Assessment and Regulation.	Yes. Minimum and maximum contents: energy, vitamins and minerals. Minimum contents: protein, carbohydrate and linoleic acid.	Yes. Swedish Food Administration.	No restrictions.	No.
U.K.	The Food Labelling Regulations 1996 (as amended) implement among others directive 89/398/EEC. Other relevant safety and consumer protection measures include UK Food Safety Act and Trade Descriptions Act 1968.	Committee on Medical Aspects of Food Policy (COMA) recommendations on the use of very low calorie diets in obesity, 1987.	Yes. Minimum contents: energy and protein, and vitamins and minerals.	No.	No restrictions.	No.

3.5. Regulation concerning product information of VLCDs in Europe

In Table 3.2. regulations concerning product information of VLCDs are listed for the various European countries. The table was constructed by means of information given by each of the participating countries. There seem to be some, albeit minor, discrepancies among countries with respect to how VLCD manufacturers are required to declare nutrient content (column 2). All countries impose that the product information must include: 1) that the product should only be used in the treatment of obesity (BMI varies from 25 to 30 kg/m^2 in those countries, which give a definition of obesity), 2) that infants, children, adolescents, pregnant or lactating women and the elderly should not use VLCDs, 3) and that it is important to maintain an adequate fluid intake (from 1.5 to 2 liter per day in those countries which quantify fluid intake). Also, all countries (except Finland) require that the consumer must be informed that VLCDs should only be used under medical supervision (column 3). Information about maximum treatment duration is not required by many countries, and varies from 1 to 4 weeks in those countries that must inform about treatment duration (column 4). Other requirements for product information are given in column 6.

Table 3.2. Regulation concerning product information of VLCDs in Europe

Country	Declaration of content	Contraindications/precautions	Maximum treatment duration	User instruction	Other requirements
Belgium	Energy in kJ and kcal per 100 g or 100 ml. Protein, carbohydrate in gram per 100 g or 100 ml. Vitamins and minerals per 100 g or 100 ml and as a percentage of RDI.	• Product can be used only for the treatment of obesity. • To be used under medical supervision. • Product use should be associated with at least 1.5 l daily of water. • Contraindicated in children and adolescents, in pregnant and lactating women, in elderly subjects, and in subjects suffering from liver and kidney diseases.	No requirements.	Must be labelled.	”Slimming product with very low energy content intended for treatment of obesity”. No indication of the speed and degree of weight loss. No indication of reduced hunger or increased satiety feelings. No indication of any effect sparing the fat free mass.
Denmark	Energy in kJ and kcal. Protein, fat and carbohydrate in g per 100 g or 100 ml, and as percentage of RDI and per daily dose. Vitamins and minerals per 100g or 100 ml and as percentage of RDI.	*”Should not be used by pregnant and lactating women”.* *”Should only be used to treat obesity”.* *”Should only be used under medical direction”.* *”Ample water intake is important”.*	No requirements.	Must be labelled.	”Slimming product with very low energy content intended for treatment of obesity”. No indication of the speed and/or degree of weight loss. No indication of reduced hunger feelings or increased satiety feelings.
Finland	Energy in kJ and kcal. Protein, fat and carbohydrate per dose and per 100 g. Vitamins and minerals per dose and per 100 g.	*”Should not be used by infants, children, adolescents and the elderly”.* *”Should not be used by pregnant and lactating women”.* *”Should only be used to treat obesity”.* *”Ample fluid intake is important”.* *”Taking the complete daily dose is important”.*	No requirements.	Must be labelled.	”Slimming product with very low energy content intended for treatment of obesity”. No indication of speed and/or degree of weight loss. No indication of reduced hunger feelings or increased satiety feeling.
France	Energy in kJ and kcal per 100 g or 100 ml . Protein, carbohydrate and fat in g per 100 g or 100 ml and as percentage of RDI and per daily dose. Vitamins and minerals per 100 g or 100 ml and as percentage of RDI.	• Must not be used in children, adolescents, pregnant and lactating women. • Only to be used for treatment of obesity (BMI>30). • To be used under medical supervision; health check before use; regularly during use: electrocardiogram and blood ionogram. • Absolute contra-indications: behavioural disorders, alcoholism, drug addiction, porphyria, cerebral arteriopathy, liver and kidney diseases, diabetes mellitus, haemopathy, cancer, electrolyte disorders, orthostatic hypotension, cardiovascular or cerebrovascular diseases and heriditary metabolic diseases. • Relative contraindications: gout, renal lithiasis and acute ischaemic cardiopathies.	Maximum use of four weeks. In case of repeated prescriptions, a period of at least 3 months with a diet supplying more than 1200 kcal must be observed between two prescriptions.	Must be labelled	A warning must clearly inform consumers that such diets can cause serious health risks if followed without advice and supervision of a physician.
Germany	No regulation.	No regulation.	No regulation.	No regulation.	No regulation.

Country	Declaration of content	Contraindications/precautions	Maximum treatment duration	User instruction	Other requirements
Ireland	Not applicable.	None.	No requirements.	Only under EU Directive 70/112/EC as amended.	None.
Italy	Energy in kJ and kcal. Protein, carbohydrate, fat, vitamins and minerals in g per 100 g or 100 ml and per daily dose.	*"Should not be used by pregnant and lactating women, and children".* *"Should only be used under medical supervision".*	*"Not to be used longer than 3 weeks, unless otherwise advised by the physician".*	Must be labelled.	"Slimming product with very low energy content intended for treatment of obesity". No indication of the speed and/or degree of weight loss. No indication of reduced hunger feelings or increased satiety feelings.
Netherlands	Energy in kJ and kcal. Protein, fat, carbohydrate and fiber in g per 100 g or 100 ml. Vitamins and minerals per 100 g or 100 ml and as percentage of RDI.	• Product intended for weight reduction. • Product for consumption under medical supervision. • This type of diet presents risks. • Ample water intake of at least 2 l daily. • Should not be used by pregnant or lactating women. • Patients with cardiovascular, pulmonary, kidney and liver diseases or depressive disorders or psychoses should consult a physician before using this type of diet. • Product is intended for the daily food supply.	Not to be used longer than 3 weeks, unless otherwise advised by the physician.	Must be labelled.	Slimming product for weight reduction.
Norway	Energy in kJ and kcal. Protein, fat and carbohydrate in g per 100 g or 100 ml. Vitamins and minerals per 100 g or 100 ml and per daily dose.	*"Ample water intake is important".* *"Should not be used by pregnant and lactating women".* *"Should not be used by children, youth or the elderly".* *"To eat the daily portion is important".* *"Should only be used to treat obesity".* *"Should only be used under medical supervision".*	*"Should not be used more than 3 weeks without medical supervision".*	Must be labelled.	"Slimming product with very low energy content intended for treatment of obesity". No indication of the speed and/or degree of weight loss. No indication of reduced hunger feelings or increased satiety feelings.
Portugal	Energy in kJ and kcal, and protein, fat and carbohydrate in g per 100 g or ml and per daily recommended dose. Vitamins and minerals per 100 g or 100 ml, and as percentage of RDI.	*"Should not be used by infants, children, adolescents, pregnant and lactating women, and elderly".* *"Should only be used under medical supervision".* *"Should have an adequate water intake".*	No requirements.	Must be labelled.	*"For the dietary management of obesity".* *"No indication of the speed and degree of weight loss".* *"No indication of reduced hunger or increased satiety feeling".*

Country	Declaration of content	Contraindications/precautions	Maximum treatment duration	User instruction	Other requirements
Sweden	Energy in kJ and kcal. Protein, fat, carbohydrate and fiber in g per 100 g or 100 ml. Vitamins and minerals per 100 g or 100 ml and as percentage of RDI.	The product shall not be used as the sole source of nutrition by individuals with severe obesity without medical supervision. The product shall not be used as the sole source of nutrition by infants, children, adolescents, pregnant or lactating women or persons with disturbed eating patterns. Further, statements of the importance of: • Eating the whole daily dose, if the product is used as the sole source of nutrition, and • Maintaining an adequate fluid intake.	The product shall not be used as the sole source of nutrition longer than 1-2 weeks.	Must be labelled.	The product must be labelled with users instructions including dosage and preparation. Net volume/weight of the product must be indicated as well as name of producer/importer. Also, a last date when the product is safe/acceptable to consume and instructions how to store the product if that has an impact on this time limit.
U.K.	Energy in kJ and kcal. Protein, carbohydrate, and fat in g per 100 g or 100 ml and per daily dose. Vitamins and minerals per 100 g or 100 ml, and per daily dose.	Manufacturers are recommended to specify absolute and relative contraindications: • Inappropriate for infants, growing children, pregnant or lactating women, and unsuitable for the elderly and those suffering from porphyria or gout. • Only to be used under medical supervision if abnormal psychological states including schizophrenia, depression of more than a minor degree, lithium therapy, behaviour disorders involving eating, alcoholism or drug abuse, heart disease, kidney disease, hypertension, cancer or diabetes treated with insulin or sulphonylureas. • Individuals with a BMI <25 should not use VLCD as a sole source of food.	Patients should not exceed the manufacturer's recommended duration (3-4 weeks) for using the product as the sole source of nourishment.	Must be labelled if impossible to make appropriate use of the food in the absence of such instructions.	None.

CHAPTER 4

VLCDs on the European market

4.1. Product information on existing VLCDs

Based on information provided by the VLCD Industry Group as well as provided by means of an inventory -based on a standardized questionnaire- that was done in each of the participating countries, a list of products with essential information could be derived. It should be emphasized that the current list may not be complete due to rapid changes in the market situation. Table 4.1. gives some basic information of products available in the participating countries. In Table 4.2. information about ingredients and nutrient content is given. Finally, information was gathered with respect to how the different products were marketed and which claims were used in the marketing of VLCDs (Table 4.3.). From column 3 it can be seen that most products have been subject to scientific documentation for efficacy and safety. A list of the scientific reports, which have appeared in peer-reviewed scientific journals (information from the producers, from scientific databases and from members of the working group) is given in Appendix 1. It can also be seen that most producers comply with regulation (from Table 3.2.) put down by each country with respect to declaration of content (column 4), contra-indications/precautions (column 5), treatment duration (column 6) and adequate user instruction (column 7).

4.2. Sales of VLCDs in Europe

Based on estimates from various market research sources including VLCD industry as well as other market research information an estimate was made on the total sales of VLCDs in the EU countries over the period 1995 to 2000 (Table 4.4.).

Table 4.1. Products, basic information

Country	Name	Producer/Importer	Type and intake	Purpose and preparation	Variants	Availability	Cost per day
Austria	Cambridge Diet	**Importer** Cambridge Diat VertriebsGmbH Josef Maybuger Kai 114 A-5020 Salzburg	Powder in measured portions 36.5 g; daily intake 109.5 g (3 portions)	Very low calorie total diet replacement for weight control. Mix with skimmed milk	Strawberry; cappuccino; vanilla; chocolate; banana; chicken & vegetable	Direct selling through consultants	7 EURO
Belgium	Modifast	**Importe***r* Novartis Consumer Health S.A.-N.V. Rue de Wandstraat 211-213 B-1020 Bruxelles	Powder in measured portions of 42 g; daily intake 126 g (3 portions. (Muesli: portions of 50 g; daily intake 150 g (3 portions).	Very low calorie total diet replacement for weight control. Mix with water.	Milkshake: vanilla; chocolate; coffee; strawberry; orange Muesli: strawberry; apple-cinnamon Soup: asparagus; bouillon Pudding: vanilla; chocolate	Pharmacy	8 EURO
	Cambridge Diet	**Importer** Cambridge Health Plan BV 3823 MK Amersfoort	Powder in measured portions of 42 g; daily intake 126 g (3 portions)	Very low calorie total diet replacement for weight control. Mix with water	Chocolate; vanilla; strawberry; banana; butterscotch; cappuccino; mushroom; vegetable; chicken & mushroom; tomato	Through consultants	7 EURO
Denmark	Nupo	**Producer** Oluf Mørk a/s Naverland 32 DK-2600 Glostrup	Powder in measured portions of 32 g; daily intake 160 g (5 portions); men are recommended 192 g (6 portions)	Very low calorie total diet replacement for weight control. Mix with water. Also meal replacement.	Chocolate; strawberry; orange. Soups: asparagus; mushroom.	Food stores and direct selling by consultants	4 EURO
	Cambridge Kuren	**Importer** Salko Import A/S Transformervej 16 DK-2730 Herlev	Powder in measured portions of 33.5 g; daily intake 134 g (4 portions)	Very low calorie total diet replacement for weight control. Mix with water.	Cocoa; vanilla; strawberry; vegetable soup; cappuccino.	Foodstores and direct selling by consultants	6 EURO
Finland	Nutrilett Intensive	**Importer** OY Nycomed Ab PL 29 FIN-02601 Espoo	Powder in measured portions of 32 g; daily intake 160 g (5 portions) for women and 192 g (6 portions) for men	Very low calorie total diet replacement for weight control. Mix with water.	Chocolate; vanilla; strawberry; bouillon.	Pharmacy; food store	8 EURO
	Nutrifast	**Producer** Leiras Oy P PL 415 FIN-20101 Turku	Powder in measured portions of 35 g; daily intake 140 g (4 portions)	Very low calorie total diet replacement for weight control. Mix with water.	Chocolate; vegetable; shrimp; bouillon.	Pharmacy; food store.	8 EURO
	Modifast	**Importer** Berner OY PL 15 FIN-00131 Helsinki	Powder in measured portions of 40 g; daily intake 120 g (3 portions).	Very low calorie total diet replacement for weight control. Mix with water.	Chocolate; vanilla; strawberry; bouillon; asparagus.	Pharmacy; food store.	7 EURO
	Dietta Mini	**Importer** OY Arla Foods PL 231 FIN-00131 Helsinki	Powder in measured portions of 35 g; daily intake 140 g (4 portions).	Very low calorie total diet replacement for weight control. Mix with water.	Vegetable; vanilla; shrimp; strawberry; chicken.	Pharmacy; food store.	7 EURO

Country	Name	Producer/Importer	Type and intake	Purpose and preparation	Variants	Availability	Cost per day
France	*Insudiet*	**Producer** Europarc BP 207 F-59654 Cilleneuve d'Ascq	Powder in measured portions à 28 g; daily intake 112 g (4 portions)	Very low calorie diet for weight control. Mix with skimmed milk	22 different flavours	Sold by direct sale only on medical supervision	7 EURO
	Cambridge Diet	**Importer** Howard Foundation France F-06800 Cagnes sur Mer	Powder in measured portions of 37.5 g daily; daily intake 112.5 g or 150 g; 3 portions for women, 4 portions for men and taller women	Very low calorie total diet replacement for weight control. Mix with water.	Banana; butterscotch; cappuccino; chocolate; chocolate mint; fruits of the forest; strawberry; vanilla; vegetable; chicken & mushroom	Diet centres and clinics	7 EURO + dietician fee.
Germany	*No products*						
Ireland	*Cambridge Diet*	**Producer** Cambridge Manufacturing Co Ltd Corby Northants NN17 1LU	Powder in measured portions of 37.5 g; 3 portions recommended per day for women and 4 for men and taller women. Also bars and Tetra Briks.	Very low calorie total diet replacement for weight control. Mix with water.	Drinks: banana; butterscotch; cappuccino; chocolate; chocolate mint; fruit of the forest; strawberry; vanilla. Soups: chicken and mushroom; vegetable	Direct selling by consultants	*Powder: 6-8 EURO* Meal bars/ Tetra Briks: 2.2 EURO
Italy	*Substi 600*	**Distributor** Abbott S.p.A. 04010 Campoverde (Latina)	Powder in measured portions à 56 g; daily intake 168 g (3 portions).	Very low calorie total diet replacement for weight control. Mix with water.	Vanilla; chocolate	Pharmacies and food stores	Has not been put on the market
Netherlands	*Modifast*	**Importer** Novartis Consumer Health B.V. Claudius Prinsenlaan, 140 NL-4818 CP Breda	Powder in measured portions of 40 g; daily intake 120 g (3 portions).	Very low calorie total diet replacement for weight control. Mix with water.	Chocolate; strawberry; coffee; vanilla; bouillon. Pudding: caramel; chocolate.	Pharmacy.	6.4 EURO
	Cambridge Diet	**Importer** Cambridge Health Plan BV 3823 MK Amersfoort	Powder in measured portions of 42 g; daily intake 126 g (3 portions)	Very low calorie total diet replacement for weight control. Mix with water.	Chocolate; vanilla; strawberry; banana; butterscotch; cappuccino; mushroom; vegetable; chicken & mushroom; tomato	Direct selling through consultants	5.8 EURO
	Weight care	**Producer** GLN Voeding BV Rietbeemdweg 1C 5705 BH Helmond	Minikuur Intensief: Three meals for five days (powder and bars): Powder in measured portions muesli of 39 g , shake of 27 g, bars of 36 g and clear soup of7 g. Minikuur Mild: Three meals for five days (powder and bars): Powder in measured portions of 27 g, bars of 58 g, creamy soup of 52 g, bars of 36 g	Very low calorie total diet replacement for weight control. Mix powder with skimmed milk. Very low calorie total diet replacement for weight control. Mix powder with skimmed milk.	Each day different flavours Each day different flavours	Pharmacy and food stores Pharmacy and food stores.	8.4 EURO 8.8 EURO

Country	Name	Producer/Importer	Type and intake	Purpose and preparation	Variants	Availability	Cost per day
Norway	*Nutrilett Intensive*	**Producer** Nycomed Pharma A/S Drammensveien 852 N-1370 Asker	Powder in measured portions of 32 g; daily intake 160 g (5 portions)	Very low calorie total diet replacement for weight control. Mix with water.	Chocolate; vanilla; strawberry; bouillon	Pharmacy	6 EURO
	Cambridge Kuren	**Importe***r* Midelfart & Co A/S 3412 Lierstranda	Powder in measured portions of 43 g; daily intake 129 g (3 portions)	Very low calorie total diet replacement for weight control. Mix with water.	Chocolate; banana; cappuccino; vegetable; chicken; tomato; strawberry	Health food stores and pharmacies	7.8 EURO
Portugal	*Micro Diet*	**Distributor** Dirvex internacional Av. Duque D'Ávila, 28-2^{0} 1000-141 Lisboa	Powder in measured portions of 58 g; daily intake 174 g (3 portions)	Very low calorie total diet replacement for weight control. Also meal replacement. Mix with water.	Chocolate; vanilla; strawberry; bouillon	Marketing networking. Pharmacies and food stores	7.5 EURO
Sweden	*Nutrilett Intensive*	**Importer** Cederroth International AB Box 715 S-19427 Upplands Väsby	Powder in measured portions of 32 g; daily intake 160 g (5 portions)	VLCD for weight control. Mix with water.	Chocolate; vanilla; strawberry; bouillon	Food stores	2.5-3.5 EURO
	Cambridge Kuren	**Importer** Cambridge Kuren Sverige AB Box 1184 SE-171 23 SOLNA	Powder in measured portions of 43 g; daily intake 129 g (3 portions)	VLCD for weight control. Also, meal replacement. Mix with water.	Banana; cappuccino; strawberry; cocoa; vanilla. Soups: Vegetables; tomato; chicken	Direct selling by consultants	5 EURO
	Modifast	**Importer** Novartis Nutrition Box 1150 SE-183 11 TÄBY	Powder in measured portions of 40 g; daily intake 120 g (3 portions)	VLCD for weight control. Also meal replacement. Mix with water.	Vanilla; tomato; asparagus; coffee; strawberry; chocolate; bouillon; orange	Pharmacy	4.5-6.5 EURO
	Ultra Diet	**Producer** Novovital AB Box 80 S- 598 22 Vimmerby	Powder in measured portions of 30 g; daily intake 90 g	VLCD for weight control. Mix with water and mix with low fat milk (100 ml)	Chocolate; strawberry	Food stores	4 EURO
UK	*Cambridge Diet*	**Producer** Cambridge Manufacturing Co Ltd Corby Northants NN17 1LU	Powder in measured portions of 37.5 g; 3 portions recommended per day for women and 4 for men and taller women. Also bars and Tetra Briks.	Very low calorie total diet replacement for weight control. Mix with water.	Drinks: banana; butterscotch; cappuccino; chocolate; chocolate mint; fruit of the forest; strawberry; vanilla. Soups: chicken and mushroom; vegetable	Direct selling by consultants	Powder: 6-8 EURO Meal bars/Tetra Briks: 2.2 EURO per bar
	Lifeline Diet	**Producer** Obesity Lifeline Ltd The Latton Bush Centre Southern way, Harlow Essex CM18 7BL	Powder in measured portions of 37.5 g and flapjack bars. 3 foodpacks recommended per day for women and 4 for men and taller women	Very low calorie total diet replacement for weight control. Mix with water/mix with ice	Drinks: banana; chocolate; raspberry; vanilla. Soups: chicken	Through counselors with MD supervision	9.4 EURO incl. Weight counselling

Country	Name	Producer/Importer	Type and intake	Purpose and preparation	Variants	Availability	Cost per day
	Lipotrim	**Producer** Howard Foundation Research Ltd. Downing Park Station Road Swaffham Bulbeck Cambs CB5 0NB	Powder in measured portions of 41.1 g. Flapjack bars. 3 foodpacks recommended per day for women, separate requirements for men	Very low calorie total diet replacement for weight control. Mix with water. Flapjack bars as meal replacement	Drinks: strawberry; chocolate; vanilla Soup: chicken Flapjacks: coconut; peanut	On referral from an MD.	5.7 EURO (women)
	Success	**Produce***r* Howard Foundation Research Ltd Downing Park Station Road Swaffham Bulbeck Cambs CB5 0NB	Powder in measured portions of 41.1 g. Flapjack bars. 3 foodpacks recommended per day for women, separate requirements for men	Very low calorie total diet replacement for weight control. Mix with water. Flapjack bars as meal replacement	Drinks: strawberry; chocolate; vanilla Soup: chicken Flapjacks: coconut; peanut	Consultant with MD supervision	9 EURO

Table 4.2. Products, ingredients and nutrient content

Country	Name	Ingredients	Energy Content		Protein Source	Protein content		Carbohydrate content		Fat	content	Vitamins and minerals
			Per 100 g	Per day		Per 100 g	Per day	Per 100g	Per day	Per 100 g	Per day	
Belgium	*Modifast*	Milk protein; milk powder, sugar, maltodextrin, minerals; sunflower oil, vitamins, thickener, sweetener and antioxidant.	380 kcal/ 1595 kJ. Muesli: 347 kcal/ 1467 kJ.	480 kcal/ 2010 kJ. Muesli: 520 kcal/ 2200 kJ.	Milk	41.0 g Muesli: 35 g	52.0 g	40.0 g; incl. 6.7 g lactose. Fiber: 0.3 g. Muesli: Fiber: 7.0 g	50.0 g; incl. 10.0 g lactose. Fiber: 0.4 g Muesli: fiber: 10.4 g	6.0 g; incl. 3.2 g linoleic and 0.2 g linolenic acid.	7.0 g; incl. 4.0 g linoleic and 0.23 g linolenic acid. Muesli: 9.0 g; incl. 3.8 g lnoleic and 0.4 g linolenic acid.	Within minimum and maximum values given by Codex (based on regulation in the Netherlands)
	Cambridge Diet	Skimmed milk powder; soya protein isolate; soya flour; soya oil, maltodextrin; sodium citrate; potassium chloride; stabiliser – xanthan gum, carrageenan; flavour; vitamin & mineral mix, magnesium oxide; sweetener - aspartame	379 kcal/ 1601 kJ.	471 kcal/ 1993 kJ.	Milk; soya	36.4 g	45.3 g	42.3 g incl. 3.4 fiber	52.7 g incl. 4.2 fiber	7.1 g	8.8 g	Based on Dutch regulation
Denmark	*Nupo*	Soy protein; vegetable fiber; skimmed milk powder; sugar; milk protein; vitamins & minerals; emulsifier; thickener (cellulose, guar, xanthan); flavourings; sweetener. Soups: Soy protein; starch; milk powder; vegetable fiber, fat powder; milk protein; vitamins & minerals; flavourings, taste enhancer.	295 kcal/ 1240 kJ. Soups: 334 kcal/ 1400 kJ.	470 kcal/ 1980 kJ. Soups: 534 kcal/ 2240 kJ.	Soy; milk	40.0 g Soups: 36.0 g	64.0 g Soups: 58.0 g	20.0 g; incl. 10 g lactose fiber: 19 g Soups: 34.0 g incl. 5 g lactose. Fiber: 10 g	32.0 g; incl. 16 g lactose Fiber: 30 g Soups: 54.0 g; incl. 8 g lactose Fiber: 16 g	6.0 g; incl. 2.0 g linoleic and 0.3 g linolenic acid.	9.5 g; incl. 3.0 g linoleic and 0.5 g linolenic acid.	Within minimum and maximum values given by Codex
	Cambridge Kuren	Skimmed milk powder; soya protein; vegetable oil; stabilizer – xanthan gum, carrageenan; flavour sweetener – aspartame; minerals; vitamins	359 kcal/ 1518 kJ.	481 kcal/ 2034 kJ	Milk; soy	38.2 g	51.2 g	37.6 g; no information on lactose. Fiber: 1.2 g	50.4 g; no information on lactose. Fiber: 1.6 g	6.2 g; incl. 2.6 g linoleic and 0.38 g linolenic	8.3 g; incl. 3.5 g linoleic and 0.5 g linolenic	

Country	Name	Ingredients	Energy Content		Protein Source	Protein content		Carbohydrate content		Fat	content	Vitamins and minerals
			Per 100 g	Per day		Per 100 g	Per day	Per 100g	Per day	Per 100 g	Per day	
Finland	*Nutrilett Intensive*	Soy protein; fructose; soy fiber; whey powder; emulsifier; sodium chloride; sodium citrate; colouring agent; thickener; sweetener; vitamins; minerals	326 kcal/ 1368 kJ.	521 kcal/ 2188 kJ.	Soy	37.7 g	60.3 g	31.5 g; incl. 5 g lactose. Fiber: 11.8 g	50;4 g; incl. 8.0 g lactose. Fiber: 18.8 g	50 g; incl. 1.8 g linoleic and 0.3 g linolenic acid	8.0 g; incl. 3.0 g linoleic and 0.5 g linolenic acid	Within minimum and maximum levels given by Codex
	Nutrifast	Milk protein; maltodextrin; oat fiber; guargum; soy protein; emulsifier; sodium chloride; sodium citrate; colouring agent; thickener; sweetener; vitamins; minerals	380 kcal/ 1600 kJ.	520 kcal/ 2200 kJ.	Milk; soy	36.0 g	52.0 g	45 g; incl. 0.5 g lactose Fiber: 3.2 g	64.0 g; incl. 0.8 g lactose. Fiber: 4.5 g	6.5 g; incl. 3 g linoleic acid; no information on linolenic acid	8.0 g; incl. 4.2 g linoleic acid: no information on linolenic acid.	
	Modifast	Casein; powdered skim milk; saccharose; maltodextrin; emulsifier; thickener; antioxidants; colouring agent; minerals & vitamins	381 kcal/ 1594 kJ.	456 kcal/ 1914 kJ.	Casein; milk protein	43.3 g	51.9 g	37.5 g; incl. 10.6 g lactose	45.0 g; incl. 12.6 g lactose	5.8 g; incl. 3.33 g linoleic acid; no information on linolenic acid	6.9 g; incl. 3.9 g linoleic acid; no information on linoleic acid	
	Dietta Minni	Milk protein; maltodextrin; oat fiber; soy oil; guargum; soy protein; emulsifier; sodium chloride; sodium citrate; colouring agent; thickener; sweetener; vitamins and minerals.	380 kcal/ 1600 kJ	520 kcal/ 2200 kJ	Milk; soy	36.0 g	52.0 g	45.0 g; incl. 0.5 g lactose. Fiber 3.2 g	64.0 g; incl. 0.8 g lactose. Fiber: 4.5 g	6.5 g; incl. 3 g linoleic acid; no information on linolenic acid	10.0 g; incl. 4.2 g linoleic acid; no information on linolenic acid	
France	*Insudiet*	Soy protein; egg powder; whey powder; emulsifier; sodium chloride; colouring agent; thickener; vitamins and minerals; fructooligosaccharides; sweetener.	363 kcal/ 1517 kJ.	408 kcal/ 1720 kJ.	Soy; egg; milk	62.0 g	75.0 g	9.2 g; incl. 0 g lactose. Fiber: 4.6 g	11.2 g; incl. 0 g lactose. Fiber: 5.6 g	8.7 g; incl. 3.0 g linoleic acid and 0.4 g linolenic acid.	10.4 g; incl. 3.6 g linoleic acid and 0.48 g linolenic acid	within minimum and maximum values given y Codex and the opinion of CEDAP

Country	Name	Ingredients	Energy Content		Protein Source	Protein content		Carbohydrate content		Fat	content	Vitamins and minerals
			Per 100 g	Per day		Per 100 g	Per day	Per 100g	Per day	Per 100 g	Per day	
	Cambridge Diet	Skimmed milk powder; soy protein isolate; soy flour; vegetable oil; vegetable oil; stabilisers (xanthan gum, carrageenan), compound vitamin & mineral mixture; flavouring; sweetener; colour; magnesium oxide, potassium chloride; trisodium citrate	363 kcal/ 1534 kJ.	Women: 408 kcal/ 1725 kJ. Men: 544 kcal/ 2300 kJ.	Milk; soy	38.5 g	Women 43.3 g Men: 57.8 g	38.0 g: incl. 29.1-35.6 g lactose Soups: 1-18.4 g lactose Fiber: 3.6 g	Women: 42.8 g; incl. 32.8-40.2 g lactose Fiber: 4.0 g Men: 57.0 g; incl. 43.7-53.4 g lactose Fiber: 5.4 g	6.3 g; incl. 3.1 g linoleic and 0.4 g linolenic acid	Women: 7.1 g; incl. 3.6 g linoleic and 0.4 g linolenic acid Men: 9.5 incl. 4.8 g linoleic and 0.5 g linolenic acid	Within minimum and maximum values given by Codex and the opinion of CEDAP
Germany	*No products*											
Ireland	*Cambridge Diet*	Skimmed milk powder; soy protein isolate; soy flour; vegetable oil; stabilisers (xanthan gum, carrageenan), compound vitamin & mineral mixture; flavouring; sweetener; colour; magnesium oxide, potassium chloride; trisodium citrate	363 kcal/ 1534 kJ	Women: 408 kcal/ 1725 kJ. Men: 544 kcal/ 2300 kJ.	Milk; soy	38.5 g	Women 43.3 g Men: 57.8 g	38.0 g: incl. 29.1-35.6 g lactose Soups: 1-18.4 g lactose Fiber: 3.6 g	Women: 42.8 g; incl. 32.8-40.2 g lactose Fiber: 4.0 g Men: 57.0 g; incl. 43.7-53.4 g lactose Fiber: 5.4 g	6.3 g; incl. 3.1 g linoleic and 0.4 g linolenic acid	Women: 7.1 g; incl. 3.6 g linoleic and 0.4 g linolenic acid Men: 9.5 incl. 4.8 g linoleic and 0.5 g linolenic acid	Complying with Directive 96/8/EC except for irond and potassium for women
Italy	*Substi 600*	Whey powder; calcium caseinate; soy fiber; corn oil; sodium citrate; potassium citrate; sugar; vitamins & minerals; emulsifier; sweetener	357 kcal/ 1500 kJ.	600 kcal/ 2520 kJ.	Milk	48.2 g	81 g	17.9 g No information on lactose and fiber	30.0 g No information on lactose and fiber	10.7 g No information on linoleic and linolenic acid.	18 g No information on linoleic and linolenic acid	Within minimum and maximum values given by Codex
Netherlands	*Modifast*	Casein; powdered skim milk; saccharose; maltodextrin; emulsifier; thickener; antioxidants; colouring agents; sweetener; vitamins & minerals	380 kcal/ 1595 kJ.	480 kcal/ 2010 kJ.	Milk	41.0 g	52.0 g	40.0 g; incl. 6.7 g lactose Fiber: 0.3 g	50.0 g; incl. 10.0 g lactose Fiber: 0.4 g	5.6 g; incl. 2.7 g linoleic and 0.4 g linolenic acid.	7.0 g; incl. 3.4 g linoleic and 0.5 g linolenic acid.	Within minimum and maximum values given by Codex

Country	Name	Ingredients	Energy Content		Protein Source	Protein content		Carbohydrate content		Fat	content	Vitamins and minerals
			Per 100 g	Per day		Per 100 g	Per day	Per 100g	Per day	Per 100 g	Per day	
	Cambridge Diet	Skimmed milk powder; soya protein isolate; soya flour; soya oil, maltodextrin; sodium citrate; potassium chloride; stabiliser-xanthan gum, carrageenan; flavour; vitamin & mineral mix, magnesium oxide; sweetener-aspartame	379 kcal/ 1601 kJ.	471 kcal/ 1993	Milk; soy	36.4 g	45.3 g	42.3 g incl. 3.4 g fiber	52.7 g incl. 4.2 g fiber	7.1 g	8.8 g	Based on Dutch regulation
	Weight Care	Minikuur Intensief		529 kcal/ 2232 kJ.	Milk, soy, pea	In the range of 17 to 25 g depending on the food item	44.5 g	In the range of 20 to 50 g depending on the food item	60.8 g; no information on lactose. Fiber: 12.6 g	In the range of 4 to 12 g depending on the food item	12.0 g	Within minimum and maximum values given by Codex (based on regulation in the Netherlands
		Minikuur Mild For both depending on the individual items (breakfast, lunch, meal soup, snack): milk protein, caseinates, whey powder, soy protein, pea protein, hydrolysed vegetable protein, dietary fibers, mono- and disaccharides, glucose and fructose/glucose syrups, vegetable oils, vitamins, minerals, fruits and fruit powders, flavourings, flavour enhancer, colourings, chocolate, cereals, cocoa powder, salt, emulsifier, thickener, stabilizer, wheat flour, lactose, starch, bouillon powder, onion powder, leek, spices, yeast extract, tomato powder, dried mushrooms, herbs, raisins, nuts, honey, sweetener		686 kcal/ 2896 kJ.	Milk, soy, pea	(breakfast bars, soup)	49.6 g		82.7 g: no information on lactose: Fiber: 16.7 g		16.9	

Country	Name	Ingredients	Energy Content		Protein Source	Protein content		Carbohydrate content		Fat	content	Vitamins and minerals
			Per 100 g	Per day		Per 100 g	Per day	Per 100g	Per day	Per 100 g	Per day	
Norway	*Nutrilett Intensive*	Soy protein; fructose; soy fiber; whey powder; emulsifier; sodium chloride; sodium citrate; colouring agent; thickener; sweetener; vitamins; minerals	326 kcal/ 1368 kJ.	521 kcal/ 2188 kJ.	Soy	37.7 g	60.3 g	31.5 g; incl. 5 g lactose. Fiber: 11.4 g	50.4 g; incl. 8 g lactose. Fiber: 18.8 g	5.0 g; incl. 1.8 g linoleic and 0.3 g linolenic acids	8.0 g; incl. 3.0 g linoleic and 0.5 g linolenic acid.	Within minimum and maximum values given by Codex
	Cambridge Kuren	Skimmed milk powder; milk protein; soya flour; emulsifier-lecithin; colouring agent; vitamin & mineral mix; thickener – xanthan gum, carrageenan; sweetener - aspartame	356 kcal/ 1505 kJ.	459 kcal/ 1942 kJ.	Milk; soy	40.1 g	51.7 g	39.7 g Fiber: 4.3 g	51.2 g Fiber: 5.5 g	6.0 g; incl. 2.9 g linoleic and 0.4 g linolenic acid	7.7 g; incl. 3.8 g linoleic and 0.5 g linolenic acid	
Portugal	*Micro Diet*	Skimmed milk; sugar; soy protein; whey powder; soy fiber; casein; emulsifier; sodium chloride; tripotassium citrate; stabilizer; calcium phosphate; vitamins and minerals; magnesium oxide; tartaric acid; sweetener; inositol	348 kcal/ 1474 kJ.	606 kcal/ 2565 k.	Milk; soy	32.3 g	56.4 g	47.0 g No information on lactose and fiber	81.9 No information on lactose and fiber	3.4 g No information on linoleic and linolenic acid	6.0 g No information on linoleic and linolenic acid	Within minimum and maximum values given by Codex
Sweden	*Nutrilett Intensive*	Soy protein; fructose; soy fiber; whey powder; emulsifier; sodium chloride; sodium citrate; colouring agent; thickener; sweetener; vitamins & minerals	335 kcal/ 1407 kJ.	535 kcal/ 2247 kJ.	Soy	37.8 g	60.3 g	31.6 g; incl. 5.0 g lactose Fiber: 11.8 g	50.4 g; incl. 8.0 g lactose Fiber: 18.9 g	5.9 g; incl. 1.9 g linoleic and 0.2 g linolenic acid	9.4 g; incl. 3.1 g linoleic and 0.5 g linolenic acid	Within Nordic Recommenda-tions
	Cambridge Kuren	Skimmed milk powder; milk protein; soya oil; mineral premix; emulsifier – lecithin; thickener – xanthan gum, carrageenan; flavour; vitamin premix; sweetener – aspartame	367 kcal/ 1552 kJ	473 kcal/ 2002 kJ.	Milk; soy	39.1 g	50.4 g	38.9 g; incl.37.3 g lactose Fiber: 4.3 g	50.2 g; incl. 48.1 g lactose Fiber: 5.5 g	6.1 g; incl. 2.9 g linoleic and 0.4 g linolenic acid	7.9 g; incl. 3.7 g linoleic and 0.5 g linolenic acid	Within Nordic Recommenda-tions

Country	Name	Ingredients	Energy Content		Protein Source	Protein content		Carbohydrate content		Fat	content	Vitamins and minerals
			Per 100 g	Per day		Per 100 g	Per day	Per 100g	Per day	Per 100 g	Per day	
	Modifast	Casein; powdered skim milk; saccharose; maltodextrin; emulsifier; thickener; antioxidants; colouring agent; minerals & vitamins	381 kcal/ 1594 kJ.	456 kcal/ 1915 kJ.	Milk	43.3 g	52.0 g	37.5 g; incl. 11.6 g lactose Fiber: <2.0 g	45.0 g; incl. 13.9 g lactose Fiber: <2.4 g	5.8 g; incl. 3.0 g linoleic and 0.01 g linolenic acid	7.0 g; incl. 3.6 g linoleic and 0.01 g linolenic acid	Within Nordic Recommenda-tions
	Ultra Diet	Soy protein; oat fiber; maltodextrin; fructose; calcium caseinate; milk powder; coconut oil (MCT fat); thickener; sweetener; colouring agent; vitamins & minerals	453 kcal/ 1900 kJ.	Powder: 408 kcal/ 1710 kJ. Total: 522 kcal/ 2190 kJ.	Soy; milk	35.3 g	Powder: 31.8 g Total: 42.3 g	60.0; incl. 2.3 g lactose Fiber: 15.0 g	Powder: 54.0 g; incl. 2.1 g lactose Fiber: 13.5 g Total: 69.0 g incl. 6.9 g lactose Fiber: 13.5 g	8.7 g; incl. 0.7 g linoleic and 0 g linolenic acid	Powder: 7.8 g; incl. 0.6 g linoleic and 0 g linolenic acid Total: 9.3 g; incl. <0.6 g linoleic and 0 g linolenic acid	In the powder alone: low levels of niacin; vitamin E; vitamin D; Na; K; Se; and I
U.K.	*Cambridge Diet*	Skimmed milk powder; soy protein isolate; soy flour; vegetable oil; stabilisers (xanthan gum, carrageenan), compound vitamin & mineral mixture; flavouring; sweetener; colour; magnesium oxide, potassium chloride; trisodium citrate	363 kcal/ 1534 kJ.	Women: 408 kcal/ 1725 kJ. Men: 544 kcal/ 2300 kJ.	Milk; soy	38.5 g	Women; 43.3 g Men: 57.8 g	38.0 g; incl. 29.1-35.6 g lactose Soups: 1-18.4 g lactose Fiber: 3.6 g	Women: 42.8 g; incl. 32.8-40.2 g lactose Fiber: 4.0 g Men: 57.0 g; incl. 43.7-53.4 g lactose Fiber: 5.4 g	6.3 g; incl. 3.1 g linoleic and 0.4 g linolenic acid	Women: 7.1 g; incl. 3.6 g linoleic and 0.4 g linolenic acid Men: 9.5 g incl. 4.8 g linoleic and 0.5 g linolenic acid	Complying with Directive 96/8/EC except for iron and potassium for women

Country	Name	Ingredients	Energy Content		Protein Source	Protein content		Carbohydrate content		Fat	content	Vitamins and minerals
			Per 100 g	Per day		Per 100 g	Per day	Per 100g	Per day	Per 100 g	Per day	
	Lifeline Diet	Skimmed milk powder; soy protein isolate; soya flour; sodium citrate; dired glucose syrup, potassium chloride; hydrogenated vegetable oil; stabilizers – xanthan gum, carrageenan; lecithin, vitamin & mineral premix; magnesium oxide; flavouring; sweetener - aspartame	360 kcal/ 1522 kJ.	405 kcal/ 1712 kJ	Milk; soy	38.2 g	43,0 g	39.1 g; incl. 30.7-34.1 g lactose Soups: 3.5 g lactose Fiber: 2.5 g	44.0 g; incl. 34.7-38.5 g lactose Fiber: 2.8 g	5.6 g; incl. 1.5 g linoleic and 0.2 g linolenic	6.3 g; incl. 1.65 g linoleic and 0.24 g linolenic acid	Complying with Directive 96/8/EC except for iron and potassium for women
	Lipotrim	Skimmed milk powder; soya flour; Soya protein isolate, acidifier – tri-sodium citrate; dipotassium posphate; vegetable oil; maltodextrin; potassium chloride; thickeners – xanthan gum, carrageenan; hydrogenated vegetable oil; mono-calcium phosphate; vitamin & mineral premix; flavouring; sweetener – aspartame; acidity regulator – potassium phosphate	368 kcal/ 1546 kJ.	Women: 425 kcal/ 1785 kJ. Men: 560 kcal/ 2350 kJ.	Milk; soy	37.2 g	Women: 42.9 g Men: 56.6 g	39.0 g; incl. 29.8-32.3 g lactose Fiber: 4.3 g	Women: 48 g; incl. 36.7-39.7 g lactose Fiber: 5.1 g Men: 59.4 g; incl. 45.3-49.1 g lactose Fiber: 6.6 g	6.1 g; incl. 3.67 g linoleic and 0.79 g linolenic acid	Women: 7.0 g; incl. 4.53 g linoleic and 0.96 g linolenic acid Men: 9.4 g; incl. 6.08 g linoleic and 1.29 g linolenic acid	Complying with Directive 96/8/EC
	Success	Skimmed milk powder; soya flour; soya protein isolate, acidifier – tri-sodium citrate; dipotassium phosphate; vegetable oil; maltodextrin;; potassium chloride; thickeners – xanthan gum, carrageenan; hydrogenated vegetable oil; mono-calcium phosphate; vitamin & mineral premix; flavouring; sweetener – aspartame; acidity regulator – potassium phosphate	368 kcal/ 1546 kJ.	Women: 425 kcal/ 1785 kJ. Men: 560 kcal/ 2350 kJ.	Milk; soy	37.2 g	Women: 42.9 g Men: 56.6 g	39.0 g; incl. 29.8-32.3 g lactose Fiber: 4.3 g	Women: 48 g; incl. 36.7-39.7 g lactose Fiber: 5.1 g Men: 59.4 g; incl. 45.3-49.1 g lactose Fiber: 6.6 g	6.1 g; incl. 3.67 g linoleic and 0.79 g linolenic acid	Women: 7.0 g; incl. 4.53 g linoleic and 0.96 g linolenic acid Men: 9.4 g; incl. 6.08 g linoleic and 1.29 g linolenic acid	Complying with Directive 96/8/EC

Table 4.3. Products, information, marketing and claims (if there is information of an exact wording of a claim, the wording is written in italic)

Country	Name	Scientific documentation	Declaration of content	Contra-indications/ precautions	Treatment duration	User instruction	Marketing	Claims
Austria	*Cambridge Diet*	Yes.	Yes.	Yes.	Yes.	Yes.	Local promotions/ word of mouth	
Belgium	*Modifast*	Yes.	Yes.	Yes.	Yes.	Yes.	No marketing	
	Cambridge Diet	Yes.	Yes.	Yes.	Yes.	Yes.	No marketing www.cambridgediet.nl.	
Denmark	*Nupo*	Yes.	Yes.	Yes.	Yes.	Yes.	Adds in sales material from supermarkets and in professional journals www.nupo.com	*"Nupo is scientifically tested by the research group in Hvidovre".* "slim" is past of the product name
	Cambridge Kuren	Yes.	Yes.	Yes.	No.	Yes.	In store promotion	Slim with safe and effective weight loss
Finland	*Nutrilett Intensive*	Yes.	Yes.	Yes.	Yes.	Yes.	Adds in newspapers. Information material available in pharmacies www.nycomed.fi/	*"your body gets important nutrients and fiber while your weight is decreasing. When you use NI your body will use own fat stores"* (on package) *"When properly used, NI will maintain your well-being, muscle strength, as your muscle mass will not diminish to any remarkable extent"* (in printed advertisements)
	Nutrifast	No.	Yes.	Yes.	Yes.	Yes.	Adds in newspapers. Information material for dieticians and physicians. Participation in commercial fares. Associated with scientific obesity meetings. www.verkkoklinikka.fi/leiras/	*"Nutrifast is developed for Finns, marketed by a drug company. It contains the protein, vitamins, and essential fatty acids your body needs. That is why you feel well and your muscles will remain well throughout the slimming"* (on package)

Country	Name	Scientific documentation	Declaration of content	Contra-indications/ precautions	Treatment duration	User instruction	Marketing	Claims
	Modifast	Yes.	Yes.	Yes.	Yes.	Yes.	Adds in newspapers. Information materials available in pharmacies	*"Balanced unique compositions enables weight reduction without symptoms usually associated with weight loss".* *"Reduces the feeling of hunger: "…is healthy, safe and effective"*
	Dietta Mini	Yes.	Yes.	Yes.	Yes.	Yes.	Adds in newspapers. Information materials available in pharmacies	*"Product is safe and enables effective and effective weight loss"*
France	*Cambridge Diet*	Yes.	Yes.	Yes.	Yes.	Yes.	Presentations and articles for health professional/consumers	
	Insudiet	No.	Yes.	No medical certificate	No.	Yes.	Only marketing focused on dieticians and MD's	Diet rich in protein, low in carbohydrate and fat
Germany	*No products*							
Ireland	*Cambridge Diet*	Yes.	Yes.	Yes.	Yes.	Yes.	Media PR/advertising and local promotion by consultants www.cambridge-diet.com	*"Bridges the gap between incorrect eating habits and an pattern of eating for life".* *"For weight loss as a sole source of nutrition for those who weight more than 1 stone (6.3 kg) to lose"* *"Worldwide has helped over 15 million people lead heal lives through effective weight management".* *"For more gradual weight loss with additional food".* *"The nutritious way to lose weight".* *"A nutritionally complete formula food which provides 100% of the Recommended Daily Allowance of all vitamins & minerals and trace elements in just over 400 kcal".*

Country	Name	Scientific documentation	Declaration of content	Contra-indications/ precautions	Treatment duration	User instruction	Marketing	Claims
Italy	*Substi 600*	No.	Yes.	Yes.	Yes.	Yes.	Marketing focused on dieticians and MD's	
Netherlands	*Cambridge Diet*	Yes.	Yes.	Yes.	Yes.	Yes.	Media PR/advertising and local promotion by consultants. Presentations to health professionals www.cambridgediet.nl	
	Modifast	Yes.	Yes.	No.	No.	Yes.	Dieticians, MD's, and general public via adds in newspapers and magazines	Modifast results in rapid and safe weight loss but does not solve the entire overweight/obesity problem. Modifast is used as part of obesity management concept
	Weight care	Yes.	Yes.	Yes.	Yes.	Yes.	Adds in magazines fair, adds in sales materials from supermarkets	Fast and effective loss of excessive weight without health risks
Norway	*Nutrilett Intensive*	Yes.	Yes.	Yes.	Yes.	Yes.	Adds in magazines	
	Cambridge Kuren	Yes.	Yes.	Yes.	Yes.	Yes.	Adds in magazines, newspaper, radio, etc. In-store promotion www.cambridgekuren.no	*"Make dream to reality – quickly"*
Portugal	*Micro Diet*	No.	Yes.	Yes.	Yes.	Yes.	Sold directly to consumers through a system of trained counsellors	Micro Diet meals are low in calories, high in nutrition. A delicious selection of healthy and convenient meal replacements enriched with vitamins & minerals
Sweden	*Nutrilett Intensive*	Yes.	Yes.	Yes.	Yes.	Yes.	Adds in newspapers www.nutrilette.cederroth.com Participation in commercial fairs associated with scientific obesity meetings	Safe and rapid weight loss
	Cambridge Kuren	Yes.	Yes.	Yes.	Yes.	Yes.	Adds in newspapers www.cambridgekuren.se Company representatives have participated in meetings with dieticians specially interested in obesity	If you follow our integrated concept we guarantee you weight loss and long-lasting change in eating habits

Country	Name	Scientific documentation	Declaration of content	Contra-indications/ precautions	Treatment duration	User instruction	Marketing	Claims
	Modifast	Yes.	Yes.	Yes.	Yes.	Yes.	Information material for MD's and dieticians. Representatives from the company take active part in meetings with dieticians interested in obesity	Modifast results in raid and safe weight loss but does not solve the entire overweight/obesity problem. Modifast is integrated in a broader weight management concept.
	Ultra Diet	No.	Yes.	Yes.	Yes.	Yes.	Adds in newspapers	Ultra diet gives you a unique opportunity to lose and maintain a lower weight without hunger. The MCT fat helps in lowering cholesterol levels and the hepatic fat metabolism
U.K.	*Cambridge Diet*	Yes.	Yes.	Yes.	Yes.	Yes.	Media PR/advertising. Local promotion by consultants. Presentations to health professionals www.cambridge-diet.co.uk	*"Bridges the gap between incorrect eating habits and a new pattern of eating for life" "For weight loss as a sole source of nutrition for those with more than 1 stone (6.3 kilos) to lose" "Worldwide has helped over 15 million people lead healthier lives through effective weight management: for more gradual weight loss with additional food" "The nutritious way to lose weight" "A nutritionally complete formula food which provides 100% of the Recommended Daily Allowance of all vitamins, minerals and trace elements in just over 400 kcal".*

Country	Name	Scientific documentation	Declaration of content	Contra-indications/ precautions	Treatment duration	User instruction	Marketing	Claims
	Lifeline Diet	No.		Yes.	Yes.	Yes.	Media advertising/PR Conferences	*"You will lose three stone in three months".* *"You will explore the reasons why you use food the way you do"* *"You will learn how to manage your weight long into the future:.* *"Fast effective weight loss; lots of support; full nutrition being with a group of others who understand; long term support".*
	Lipotrim	No.	Yes.	Yes.	MD decision	Yes.	Marketing focused on MD's obesity@lipotrim.demon.co.uk	*"Weight loss phase… patients can be expected to lose weight at a consistent rate of around 1 stone (6.4 kg) per month".* *"An ideal option for hypertensive patients and those with NIDDM. Weight loss will generally alleviate these symptoms".*
	Success	No.	Yes.	Yes.	Yes.	Yes.	To healthy obese	*"Weight loss phase.. patients can be expected to lose weight at a consistent rate of around 1 stone (6.4 kg) per month"*

Table 4.4. Sales volume in person months used

YEAR	SALES VOLUME PERSON MONTHS SUPPLY ('000s)
1995	107.1
1996	87.2
1997	80.3
1998	70.5
1999	65.1
2000	67.8

[based on industry estimates]

CHAPTER 5

Obesity

5.1. Introduction

Obesity has been one of the most intensive health concerns of people in industrialized countries for decades. However, in recent years it has also been recognized as a rapidly growing threat to the health of inhabitants from countries all over the world. It is considered nowadays as a chronic disease with a significant contribution to ill health. Although the origin of the disease is simple in theory: namely a positive energy balance either by excess intake or reduced expenditure or both, its treatment is complex and so far not very successful. Many factors influence the development of obesity. Each of these is influenced by a variety of individual factors reflecting genes and metabolism, which are in turn modified by environmental and social factors. The current epidemic of overweight, however, must be largely environmental based on changes in food habits and daily physical activity. The ancient genetic make up is the product of survival when food scarcity was the rule. The nation wide mismatch between food and energy, 'people eat what they need', is only from recent years. The argument that the epidemic of overweight is largely environmental, is important because it helps direct strategies for prevention and treatment.

This chapter will review shortly some aspects on the prevalence of obesity, its health consequences and its economic costs. Finally, the dietary treatment as management tool in the treatment of obesity will be discussed.

5.2. The prevalence of obesity in Europe

Overweight (BMI $\geq$ 25 kg/m^2) and obesity (BMI $\geq$ 30 kg/m^2) are common in all European countries, and the prevalence is still increasing. About half of European men and 30-40% of women are overweight, and about 15-30% of the adults are obese. The prevalence tends to be higher in the eastern parts of central Europe than in the western parts and Scandinavia (Table 5.1.).

Table 5.1. Data on prevalence (%) of overweight and obesity in different European countries, as published in the European Cardiovascular Disease Statistics, 2000

		MEN		WOMEN	
MONICA Population	**Year of Survey**	**Overweight BMI > 25**	**Obese BMI > 30**	**Overweight BMI > 25**	**Obese BMI > 30**
Belgium - Charleroi	1990/93	47	19	33	24
Belgium – Ghent	1990/93	52	13	40	16
Czech Republic	1992	52	23	35	30
Denmark – Glostrup	1991/92	41	13	26	12
Finland – Kuopio Prov.	1992	46	24	34	26
Finland – North Karelia	1992	49	23	37	24
Finland – Turku/Loimaa	1992	46	22	35	19
France – Lille	1995/96	40	17	30	22
France – Strasbourg	1995/97	51	22	31	19
France – Toulouse	1994/96	49	13	24	10
Germany – Augsburg (rural)	1994/95	55	24	33	23
Germany – Augsburg (urban)	1995	54	17	36	21
Germany – Berlin Lichtenberg	1988	49	13	36	14
Germany – Bremen	1991/92	50	16	36	19
Germany – Cotbus County	1989/90	56	19	35	21
Germany – East Germany	1993/94	49	16	34	20
Germany – Halle county	1988/89	53	18	34	26
Germany – Karl Marx Stadt County	1988/89	51	15	36	21
Hungary – Budapest	1987/89	46	23	36	28
Hungary – Pecs	1987/89	40	22	36	29
Italy – Area Brainza	1993/94	50	14	29	18
Italy – Fruili	1994	51	17	31	19
Poland – Tarnobrzeeg Voivodshiip	1992/93	41	15	36	36
Poland – Warsaw	1993	45	22	35	29
Spain – Catalonia	1994/96	53	16	42	25
Sweden – Gothenburg	1994/96	47	13	31	10
Sweden – Northern Sweden	1994	50	14	34	14
Switzerland – Ticino	1993	53	13	27	16
Switzerland – Vaud/Fribourg	1992/93	47	16	31	10
UK Belfast	1991/92	49	14	30	16
UK Glasgow	1995	42	23	36	23
Yugoslavia – Novi Sad	1994/95	49	20	36	32
Other studies					
Estonia	1997	32	10	24	6
Latvia	1997	41	10	33	17
Lithuania	1997	42	11	33	18
Ireland	1998/2000	46	20	33	16
Finland	1997	48	20	33	19

[adapted by Rayner and Petersen; published by the British Heart Foundation]

5.3. Prevalence of childhood obesity in Europe

Childhood obesity is nowadays being recognized as a growing public health problem in Europe. Longitudinal studies have indicated that childhood obesity is an important predictor of adult obesity, particularly during the second decade of life. Especially extremely overweight children of obese parents seem to be at risk. Having acknowledged that childhood obesity is indeed an important public health issue, scientific research is now focussing on the treatment and prevention of childhood obesity.

An important and crucial point is the definition of childhood obesity. In a recently published paper of Cole and co-workers (2000) standard definitions for childhood overweight and obesity were developed. As proposed by the International Obesity Task Force, the adult cut-off points -a BMI of 25 kg/m^2 for overweight and 30 kg/m^2 for obesity- were linked to centiles of BMI for children, in order to provide childhood cut-off points. Data were obtained from six large nationally representative cross-sectional surveys on growth from Brazil, Great Britain, Hong Kong, The Netherlands, Singapore, and The United States. The total sample size was 97,876 males and 94,851 females from birth to 25 years of age. For each of the surveys, centile curves were drawn that at age 18 years passed through the adult cut-off points of 25 and 30 kg/m^2. The resulting curves were averaged to provide age and sex specific cut-off points for 2-18 years. The approach used in this international survey avoids some of the usual arbitrariness of choosing the reference data and cut-off points. Therefore, direct comparison of trends in childhood obesity worldwide is facilitated.

The available literature regarding the prevalence of childhood obesity is described in detail by Livingstone (2000) and summarized in Table 5.2. An important factor in the analysis of the results is the design of the study. Monitoring secular trends in the prevalence of obesity in European children and adolescents are ideally studied by longitudinal datasets which mirror the ethnic and socio-economic composition of the population. Unfortunately, there are only few prospective longitudinal studies with respect to childhood obesity. Another way of investigating childhood obesity is by means of cross-sectional studies, although it has limitations (momentary state of condition, no tracking of individual development of adiposity, no clarity about cause and effect). Taking the pros and cons of the different study approaches into account, complex patterns appear varying with time, age, sex and geographical region. The overall pattern suggests that prevalence rates in young children are relatively low compared to adolescents. Gender differences in the prevalence of obesity are inconsistent. The most obvious trend however, is the considerable geographical variation in the prevalence of childhood obesity. Obesity is most frequently observed in the eastern European countries, particularly Hungary, and the southern European countries, like Italy, Spain and Greece. In contrast, northern European countries tend to have lower rates and these are broadly comparable across countries.

Table 5.2. Prevalence of overweight and obesity in European children and adolescents

Country	Age (y)	Number (m, f)	Study design	Body fat index	Prevalence (%)
Austria					
Elmadfa et al., 1993	7-18 y	1120 m, 1190 f	Cross-sectional	RBW > 120 %	19-29 % (m), 13-17 % (f)
Belgium					
De Spiegelaere et al., 1998	12-15 y	1268 m, 1339 f	Retrospective cohort	BMI > 120 % of median BMI > 140 % of median	20-21 % 6 %
Bulgaria					
Damyanova et al., 1979	0-7 y	3494	Cross-sectional	RBW > 110 % RBW > 120 %	7-8 % 3-6 %
Finland					
Nuutinen et al., 1991	3-18 y 1980: 1983: 1986:	 1764 m, 1832 f 1403 m, 1485 f 1186 m, 1317 f	Prospective longitudinal	TSF > 90th percentile TSF > 90th percentile and BMI > 90th percentile	 1980: 1-12 % (m), 4-9 % (f) 1983: 7-16 % (m), 8-10 % (f) 1986: 5-13 % (m), 2-7 % (f) 4 % (m), 2-7 % (f)
Pietiläinen et al., 1999	16-17 y 16 y: 16.5 y: 17 y:	 2299 m, 2585 f 1147 m, 1362 f 2202 m, 2399 f	Cross-sectional and longitudinal	BMI > 25	 16 y: 4 % (m), 4 % (f) 16.5 y: 9 % (m), 5 % (f) 17 y: 6 % (m), 5 % (f)
France					
Bellisle et al., 1988	7-12 y	339	Cross-sectional	BMI > 85th percentile BMI > 97th percentile	12 % 14 %
Germany					
Deutsche Gesellschaft für Ernährung (DGE), 2000	6-16 y	733 m, 756 f	Cross-sectional	BMI > 90th percentile BMI > 97th percentile	12 % (m), 10 % (f) 14 % (m), 12 % (f)
Greece					
Kafatos et al., 1981	10-15 y	567 m, 543 f	Cross-sectional	RBW > 95th percentile	33 % (m), 36 % (f)
Hungary					
Bihari and Bedö, 1982	7-18 y	5139 m, 4871 f	Cross-sectional	RBW > 120 %	4-8 % (m), 4-8 % (f)
Biró, 1993	15-18 y	171 m, 237 f	Cross-sectional	BMI > 25	11 % (m), 9 % (f)
Czinner et al., 1983	7-15 y	336 m, 305 f	Cross-sectional	Body fat > 25 % (m) or > 30 % (f)	16 % (m), 15 % (f)
Dóber, 1987	6-18 y	1500 m, 1574 f	Cross-sectional	TSF > 90th percentile	13 % (m), 10 % (f)
Wilhelm and Csombók, 1983; 1984	1-14 y	8040 m, 7973 f	Cross-sectional	RBW > 110 %	2-10 % (m), 1-8 % (f)

Country	Age (y)	Number (m, f)	Study design	Body fat index	Prevalence (%)
Italy					
Beccaria et al., 2000	6-12 y	3742 m, 3549 f	Cross-Sectional	120 % < RBW < 140 % RBW > 140 %	17 % (m), 13 % (f) 7 % (m), 4 % (f)
Capozzi et al., 1989; Cerrati et al., 1990; Giovannini et al., 1986; Pinelli et al., 1987; Zoppi and Bressan, 1990	3-13 y	64,770	Cross-Sectional	RBW > 120 %	1-18 %
Maffeis et al., 1993	4-12 y	749 m, 774 f	Cross-Sectional	RBW > 110 % RBW > 120 %	11-18 % (m), 2-15 % (f) 4-23 % (m), 2-13 % (f)
Maffeis et al., 1998	8, 12 y 1992: 1996:	 298 112	Prospective longitudinal	RBMI > 120 %	 1992: 21 % (m), 28 % (f) 1996: 19 % (m), 21 % (f)
Netherlands					
Hoffmans et al., 1988	18 y	78,612	Prospective longitudinal	BMI: 25-29.9	1.8 %
Van Poppel et al., 1991	10-11 y	126 m	Cross-Sectional	BMI > 97th percentile	8 %
Spain					
Moreno et al., 1998	6-7 y 13-14 y	90,997 106,284	Cross-Sectional	BMI > 95th percentile	1985: 3-6 % (m), 1-10 % (f) 1995: 6-14 % (m), 2-18 % (f)
Sweden					
Mellbin and Vuille, 1976	7, 10 y	459 m, 504 f	Prospective longitudinal	RBW > 110 % RBW > 120 %	10 % (m), 8-13 % (f) 3-4 % (m), 4-6 % (f)
Persson et al., 1989	4, 8, 13 y 1967: 1980:	 1411 572	Cross-Sectional	RBW > 120 %	 1967: 3-7 % 1980: 3-11 %
United Kingdom					
Colley, 1974	6-14 y	1243 m, 1183 f	Cross-Sectional	TSF > 25 mm	2 % (m), 6 % (f)
Hackett et al., 1997	13-14 y	1150	Cross-Sectional	BMI > 25 BMI > 30	6 % 2 %
Peckham et al., 1983	7-16 y 1946: 1958:	 3934 36,835	Prospective longitudinal	RBW > 120 %	 1946: 2-7 % (m), 4-10 % (f) 1958: 4-8 % (m), 6-10 % (f)
Poskitt and Cole, 1978	4-6 y	203	Prospective longitudinal	RBW > 110 %	1 %
Power et al., 1997	7, 11, 16 y	18,953 m, 17882 f	Prospective longitudinal	BMI > 91th percentile BMI > 95th percentile BMI > 98th percentile	5 % (m), 4-5 % (f) 3 % (m), 2-3 % (f) 1 % (m), 1 % (f)
Shukla et al., 1972	0-1 y	300	Cross-Sectional	RBW > 110 % RBW > 120 %	28 % 17 %
Stark et al., 1981	6-26 y 6, 7, 11, 14 y 20, 26 y	 3949 3520	Prospective longitudinal	RBW > 120 %	 2-7 % (m), 3-10 % (f) 5-12 % (m), 7-11 % (f)

BMI = body mass index; RBMI = relative body mass index; RBW = relative body weight; TSF = triceps skinfold thickness [adapted from Livingstone, 2000]

5.4. Health risks of obesity

The severity of obesity is commonly estimated from the body mass index (BMI): an index that attempts to normalize for height, thereby permitting comparison of the transformed weights of individuals of different statures. BMI is determined by dividing weight in kg by the square of the height in meters. It is helpful to have a frame of reference by which to assess degree of overweight.

Table 5.3. Categories of overweight in adults according to BMI

Classification	BMI (kg/m^2)	Risk of co-morbidities
underweight	< 18.5	increased
normal range	18.5 - 24.9	average
overweight	25 - 29.9	increased
obese class I	30 - 34.9	moderate
obese class II	35 - 39.9	severe
obese class III	$\geq$ 40	very severe

[WHO, 1998]

The BMI embodies both the fat and fat-free components of the body: it is therefore an index for weight and not for fatness as such. BMI is a useful measure of obesity since on population level it correlates reasonably well with the body fat mass.

Classification of obesity is of importance for a number of reasons:

- to identify individuals at increased risk for morbidity and mortality;
- to select intervention therapy at individual and population levels;
- as basis for evaluating interventions.

Besides the BMI as index for obesity and related co-morbidities, other indexes have been proposed in relation to the severity of the health consequences of obesity. Waist-hip relation (W/H >1.0 in men and >0.85 in women) has been accepted as an alternative simple measure to identify patients with abdominal fat accumulation (WHO, 1998). Especially abdominal fat accumulation is considered as a risk for obesity related co-morbidity.

More recently, waist circumference is proposed and very well received as a convenient and simple measurement and as an approximate index of intra-abdominal fat mass and total body fat (Lean et al., 1995). Furthermore, changes in waist circumference reflect changes in risk factors for cardiovascular disease (CVD) (Han et al., 1997). From a study in The Netherlands sex-specific waist circumferences were derived in relation to co-morbidity risks (Table 5.4.).

Table 5.4. Risk of obesity co-morbidity in relation to waist circumference

Classification	Increased	Substantially increased
men	≥ 94 cm	≥ 102 cm
women	≥ 80 cm	≥ 88 cm

[Han et al., 1995]

Overweight and obesity are associated with increased risks for a number of clinically important chronic related conditions. The most serious of these conditions affect mortality. The major health consequences associated with overweight and obesity are non-insulin-dependent diabetes mellitus (NIDDM), coronary heart disease (CHD), hypertension, gall bladder disease, psychosocial disturbances and certain types of cancer. Based on a number of epidemiological studies, the WHO presented an estimation of relative risks of health problems associated with obesity (Table 5.5.).

Table 5.5. Relative risk of health problems associated with obesity

Greatly increased (relative risk much greater than 3) [a]	Moderately increased (relative risk 2-3) [a]	Slightly increased (relative risk 1-2) [a]
NIDDM	CVD	cancer (breast cancer in postmenopausal women, endometrial cancer, colon cancer)
gall bladder disease	hypertension	reproductive hormone abnormalities
dyslipidaemia	osteoarthritis (knees)	polycystic ovary syndrome
insulin resistance	hyperuricaemia and gout	impaired fertility
breathlessness		low back pain due to obesity
sleep apnoea		increased anaesthetic risk
		fetal defects associated with maternal obesity

[a] all relative-risk estimates are approximate [WHO, 1998]

Especially those relative risks higher than 2-3 can be considered as serious health related risks. A number of them are mechanical in origin, such as breathlessness, snoring, sleep apnoea, decreased vital capacity, knee and hip arthritis and increased risk of accidental

injuries. In addition, in a Finnish study it was found that one-quarter of all disability pensions for CHD and musculo-skeletal causes in women and one-eighth of those in men could be attributed to the recipient being overweight (Rissanen et al., 1990).
It is generally accepted that intra-abdominal fat accumulation has a much higher risk for most of the listed co-morbidity compared to fat accumulation in the extremities, especially insulin resistance and the metabolic syndrome (hyperinsulinaemia, dyslipidaemia, glucose intolerance and hypertension).

Obesity related co-morbidities affect mortality

Already in the fifties insurance companies used the height-for-weight mortality tables as a proxy for mortality risks. Based on these large-scale cohorts, the first so-called U- or J-shaped associations were published. There has been much controversy about the curves, especially in relation to confounding factors such as cigarette smoking, illness related weight loss, etc. After an extensive analysis of several studies the American Institute of Nutrition came to the conclusion that the lowest mortality risk is associated with a BMI between 18 and 25 kg/m^2 (Blackburn and Kanders, 1994). From a BMI of 25 kg/m^2 an almost linear and continuous relationship between BMI and mortality is found. In younger age groups (<50 years) this relationship is steeper with increasing BMI compared to older age groups (>50 years).

For a detailed description of the relation between obesity and the different co-morbidities, one is referred to the Report of a WHO Consultation on Obesity (1998).

5.5. Health care costs of obesity

Obesity has wide-reaching medical, social and economical consequences (WHO, 1998). Excess body weight is associated with a number of chronic diseases and functional limitations. The direct costs of diagnosing and treating diseases related to overweight and obesity are estimated to be in the order of 2–8% of total national health care costs, amounting to an estimated 70 billion dollars in 1995 in the US alone (Colditz, 1999). In Table 5.6. the health care costs for a number of countries are depicted. Indirect costs denoting costs of the loss of productivity due to premature work disability and mortality may be even higher. Sustained weight reduction would probably reverse these trends (Oster et al., 1999).

Table 5.6. Direct costs of obesity

Study	**Country**	**% of health expenditure care**
Colditz, 1992	USA	5.5 %
Segal et al., 1994	Australia	2.0 %
Seidell, 1995	The Netherlands	3.0 %
Lévy et al., 1995	France	2.0 %
Swinburn et al., 1997	New Zealand	2.5 %
Wolf and Colditz, 1998	USA	5.7 %
Birmingham et al., 1999	Canada	2.4 %
Pereira et al., pers. comm.	Portugal	3.5 %

The costs of health care that are attributed to obesity are described in more detail for Germany as an example. To estimate the costs the 1990 health care costs of coronary heart disease, hypertension, non-insulin-dependent diabetes, gallstone disease, gout, hyperlipidemia, cancer of prostate, breast cancer, endometrial cancer and colon cancer were calculated using data from a variety of sources. The fraction of these costs attributable to obesity was estimated using relative risk (or attributable risk) estimates of these conditions in obesity. As shown in Table 5.7., two models were used to estimate the costs. The more conservative model I uses the lower range and model II uses the higher range of risk estimates and attributable risks taken from the literature. As the overall costs depend on the prevalence of obesity, two alternative prevalences (12% and 18%) were used in both models (Schneider et al., 1996).

Table 5.7. Attributable risks of obese subjects using different models

	MODEL					
	Ia		Ib	IIa		IIb
Coronary heart disease		70%			70%	
Hypertension		66%			77%	
Type 2 diabetes mellitus		66%			94%	
Gallbladder disease		50%			90%	
Gout		60%			60%	
Hyperlipidemia		33%			33%	
Prostate cancer		0%			90%	
Breast cancer		17%			23%	
Endometrial cancer		0%			30%	
Colon cancer		23%			23%	
Prevalence of obesity	12 %		18%	12%		18%

Model I: Low estimate of attributable risks with prevalence of obesity at 12% (model Ia) and 18% (model Ib)

Model II: High estimate of attributable risks with prevalence of obesity at 12% (model IIa) and 18% (model IIb)

[adapted from Schneider et al., 1996]

These two modelling techniques yield somewhat different results for the health care costs. The components of the costs include direct costs resulting from treatment of morbidity of the conditions listed above and indirect costs caused by lost productivity (work days lost) and forgone earnings caused by premature mortality.

The total obesity costs were estimated to range from 3.1 to 5.5% of total health expenditures in West-Germany and from 5.9 to 10.4% in East Germany (Table 5.8.). Altogether the economic impact of obesity on the Federal Republic of Germany was estimated to range between 11.1 and 19.3 billion German marks (DM) in 1990. These results were remarkably similar to reports on the economic costs of obesity in other western countries (Table 5.6.).

Table 5.8 Health care costs of obesity in Germany

	MODEL			
	Ia	Ib	IIa	IIb
Prevalence	12%	18%	12%	18%
West-Germany	**Costs (in million DM)**			
	4143	5333	6101	7691
	4490	5989	5713	7338
	8633	11523	11814	15030
	3.1%	4.2%	4.3%	5.5%
East-Germany	**Costs (in million DM)**			
	1206	1611	1776	2239
	1261	1682	1609	2066
	2467	3293	3385	4305
	5.9%	7.9%	8.2%	10.4%

[adapted from Schneider et al., 1996]

In conclusion, based on the existing information from different western countries, obesity represents a major avoidable contributor to the cost of illness in affluent countries.

5.6. Health benefits of weight loss

Weight loss is known to reduce obesity related disease risks and to improve or resolve co-morbid disorders. Weight loss in obese persons may not extend their life span but can improve other intermediate measures of their health status and overall quality of life. In the vast majority of weight loss studies however, only associations with mortality have been examined. A few studies have included measurements of disease incidence or morbidity.

In two reviews, data from 19 epidemiological studies on the association between weight loss and active average life expectancy were examined (Andres et al., 1993; Blair et al., 1993). In 6 of these studies a positive benefit of weight loss on mortality was found. Especially, the 1950 Metropolitan Life Insurance Study showed convincing and positive results, that formerly obese persons who had been 're-rated' for life insurance at a lower premium because they had lost weight, experienced substantially lower mortality rates over a 16 to 25 year period of time than did their counterparts, who had remained obese. Former moderately overweight men and women had 20% and 37% lower mortality rates respectively and severely obese men and women had 39% and 16% lower mortality rates

respectively. In contrast, the results of the remaining 13 studies showed either inconsistent associations between weight loss and longevity or consistent deleterious associations.
It is expected that the ongoing Swedish Obese Subjects (SOS) study, where obese patients are either allocated to conventional dietary treatment or to surgical treatment, will give us valuable information about the health benefits of successful long-term maintenance of extensive weight loss (Sjöström, 2000).

Weight loss as low as 5% of body weight has been shown to reduce or eliminate disorders associated with obesity and a 10% to 20% reduction in body weight with maintenance of this weight loss over 2 to 5 years can reduce health risks and maintain health benefits. Most obese patients can achieve this weight loss in 12 to 16 weeks on a balanced hypocaloric diet or on a VLCD combined with regular exercise and behaviour modification and this degree of weight loss can be maintained for 1 to 2 years.
Successful treatment of obesity should therefore not only be defined as long-term weight maintenance of a desired weight but should also focus on the amount of weight loss necessary to promote health and prevent diseases - reasonable yet targeted weight loss goal (Weighing the options, 1995).

5.6.a. NIDDM

While the interactions between obesity and NIDDM remain unclear, weight loss has been shown clearly to ameliorate insulin resistance, improve carbohydrate tolerance, and reduce hyperglycemia and hyperinsulinemia. Mostly hyperglycemia lessens as soon as a hypocaloric diet is initiated, suggesting that energy restriction has a beneficial effect, independent from weight loss. Furthermore, several studies have shown that a weight loss of 10 to 20% greatly improves glycemic control of NIDDM subjects and that such improvement can last from 1 to 3 years, even if some weight is subsequently regained. Also, medication in NIDDM can be stopped in most cases already during the hypocaloric (VLCD) period (Wadden and Stunkard, 1993).
Weight loss improves many of the concomitant metabolic abnormalities predisposing to the complications of diabetes. Weight loss may reduce mortality of obese type 2 diabetics (Williamson et al., 2000). Loss of a modest amount of weight (over 4 kg) has recently been shown to greatly reduce the risk of developing diabetes in high risk people (Tuomilehto et al., 2001). The protective effect of weight loss may extend over several decades if the weight loss is sustained (Moore et al., 2000).

5.6.b. Cardiovascular disease

Obesity is associated with elevated triglyceride levels, lowered high-density (HDL) cholesterol levels and increased LDL/HDL cholesterol ratio, which entail the greatest risks for arteriosclerosis. Even modest weight loss of 5 to 10% is associated with an increase in HDL cholesterol and an improvement of the ratio (Yu-Poth et al., 1999). Also, it has been

found that serum triglyceride and HDL cholesterol levels show the most favourable changes after weight loss in those with a high waist-hip ratio (WHO, 1998).
Furthermore, hypertriglyceridemia is reversible to weight loss. In the recent debate about the fat/carbohydrate ratio in the diet and weight loss, arguments were put forward against the reduction of fat intake in relation to obesity due to the HDL cholesterol lowering effect of an equicaloric exchange of fat to carbohydrate (Katan et al., 1998). However, the concomitant decrease of weight and increase of HDL cholesterol levels will counterbalance the decreasing effect of a low fat / carbohydrate ratio in the diet (Saris et al., 2000).

5.6.c. Gall stone formation

There have been reports on the relation between energy restriction and thus weight loss and gall stones. Obesity in itself is already known for the increased risk for gallstones, especially in women. Energy restriction in the obese population will yield a higher risk for gallstones. The mechanism of the increased risk during energy restriction includes super-saturation of bilary cholesterol and gall bladder stasis. Diets that provide 15 g of protein and 5 g of fat in at least one meal daily (to ensure adequate gall bladder contraction) reduce or eliminate the risk for gallstones formation (Blackburn and Kanders, 1994). The VLCD situation is considered in Chapter 8.2. If the daily fat component of VLCD is 7 g or above, cholelithiasis is no greater problem than that encountered with any weight reduction programme. Reduced-obese patients have a risk that is comparable to that in the non-obese population.

5.6.d. Sleep apnoea

Modest weight loss (9%) has been shown to reduce the frequency of apnoea, to improve sleep quality and to reduce daytime somnolence. Although the exact mechanism remains unknown, such improvements might result either from changes in the anatomy of the airway or from changes in the ventilatory drive.

5.6.e. Psychosocial functioning

One of the most rewarding areas of improved function after weight loss, is the area of psychosocial functioning. A large number of studies, including studies with surgical treatment, showed dramatic improvement of self-esteem, mental well being, levels of anxiety, and depression as well as social interaction (Wadden and Stunkard, 1993).

5.6.f. Weight fluctuation

In the last decade a number of prospective studies has been published on the effects of weight cycling and mortality/morbidity. In some of these studies an increased risk for morbidity and mortality was observed. The major concern in all of these large-scale epidemiological studies is the problem how to identify intentional weight loss separate from unintentional weight loss, which is most probably linked to existing diseases.
The US National Task Force on The Prevention and Treatment of Obesity concluded that the available evidence at that time was not sufficiently compelling to override the potential

benefits of weight loss in obese patients (National Task Force, 1993). The eight year follow-up of the SOS study showed that the surgical treated group who lost 20 to 30 kg in weight, gained substantial health benefits (Sjöström, 2000).

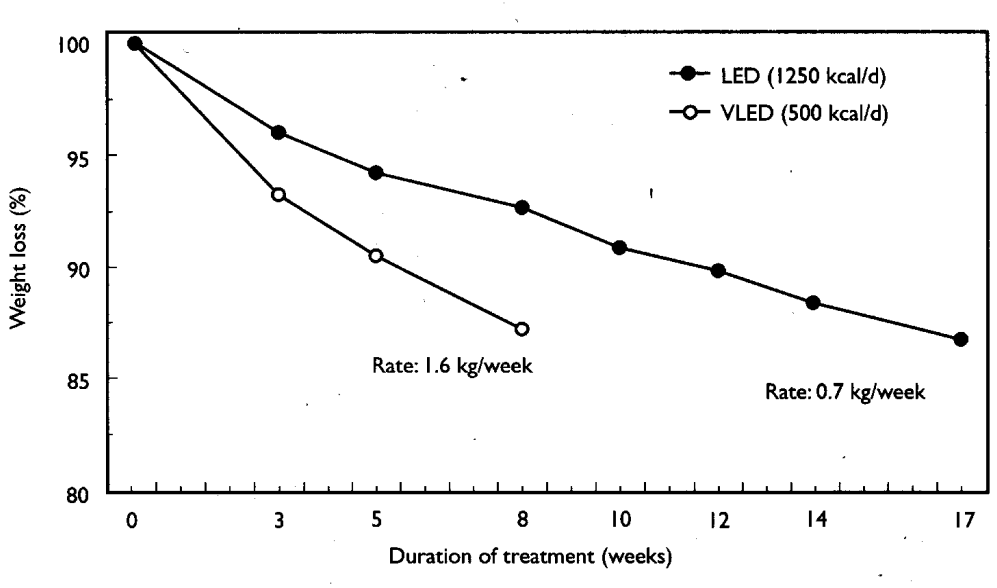
5.7. Dietary treatment modalities and efficacy

Dietary treatment is one of the cornerstones of a weight loss programme. It consists basically of an instruction to patients how to modify their dietary intake to achieve a decrease in energy intake while maintaining a nutritionally adequate diet. Overweight and obese patients have, due to their enlarged body size, higher energy requirements at a given level of physical activity compared to their lean counterparts. Already the reduction of energy intake of an obese patient to that of a normal weight individual will cause weight loss, consisting of about 75 % fat and 25 % lean tissue until weight normalization occurs at a new equilibrium (Van Gaal, 1998). For obese subjects (BMI 30 - 35 kg/m^2) this requires an energy deficit of 300-500 kilocalories per day and for patients with severe obesity (BMI > 40 kg/m^2) an energy deficit of 500-1000 kilocalories per day (Garrow, 1978).
So far the scientific literature does not support the idea that differences in dietary composition exert clinically important effects on energy expenditure. Diets high in protein (25 energy %) do have an effect on energy balance due to a higher satiety effect and diet induced thermogenesis leading to a weight loss of about 4 kg (Skov et al., 1999). This level of change in body weight is of importance in relation to preventive measures to reduce the prevalence of obesity in a population, but has no clinical relevance in the individual obese patient who wants to lose 5 to 10 % body weight.

To prescribe a diet with a defined energy deficit, it is necessary to have an estimate of the patients' actual energy requirements. Due to the invalid estimation of the energy intake in obese patients, energy requirements should therefore be assessed indirectly by the estimation of the total energy expenditure. This total energy requirement is estimated from a calculated or measured RMR multiplied with an activity factor.
Therapeutic obesity diets distinguish between several recognized weight reduction regimens. Low calorie diets (LCD) usually provide 800-1500 kilocalories per day. Diets providing 1200 kilocalories per day or more may be classified as balanced deficit diets (WHO, 1998). Very low calorie diets are modified fasts providing up to 800 kilocalories per day.
VLCD aim to supply little energy but all the essential nutrients. Reducing the energy content of a diet requires an increased nutrient density. This can be difficult to obtain with natural food. In contrast LCDs normally consist of natural food. LCDs are also called calorie-counting diets because more emphasis was previously put on restricting the energy intake level and less on macronutrient composition. Although the macronutrient composition is of less importance for short-term weight loss, it is now usually also

modified to maximize the beneficial effect on cardiovascular risk factors and insulin resistance and to change dietary habits for long-term weight maintenance. LCD diets are low fat / high carbohydrate diets frequently supplemented with a vitamin and mineral tablet. Formulated LCDs have mostly a similar nutrient composition compared to VLCD except for energy. There is of course a difference in the rate of weight loss between LCD and VLCD as can be seen in Figure 5.1. based on a study from Toubro and Astrup (1997).

Figure 5.1. Weight loss curves on a LCD and VLCD diet



[Toubro and Astrup, 1997]

Related to the issue of dietary composition and obesity it has become clear that an ad libitum low fat diet is of importance to reduce the problem of obesity. Data from animal and experimental research as well as numerous observational studies and randomized controlled trials (RCTs) have shown that high fat diets play an important role in the development of obesity. The main mechanisms are the passive over-consumption of energy and a reduced fat oxidation capacity, most probably caused by low levels of physical activity and fitness. A systematic review of ad libitum low fat RCTs with duration of 2 to 12 months showed a 3.2 kg greater weight loss. This weight loss is more substantial in heavier subjects (Astrup et al., 2000).

Analysis indicates that obese patients (BMI > 30 kg/m^2) with a body weight of 95 kg who reduce dietary fat from 45 to 25 energy % under ad libitum conditions will reduce their energy intake and will on average achieve a weight loss of 5-7 kg before a new equilibrium is reached. On the other hand, a normal weight subject (70 kg) will lose only 0.5 kg with the same fat reduction.

The target of a weight loss programme should initially be to decrease body weight by about 10% (WHO 1998). Once this has been achieved, a new target can be set. Patients will generally want to lose more weight, but it should be remembered that even a 5 % weight reduction improves risk factors and the risk of co-morbidity. If on the other hand expectations are not achieved, the compliance to the diet will be minimal.

Recently, it was suggested by Astrup and Rössner (2000) that an initial greater weight loss improves long-term maintenance. In contrast to the common belief that weight loss achieved at a slow rate is better preserved than if the weight is lost more rapidly, the literature shows that initial weight loss is positively, not negatively, related to long-term weight maintenance. There is evidence from randomized controlled intervention trials to support the view that a greater initial weight loss induced without changes in lifestyle (e.g. VLCDs or anorectic drugs) improves long-term weight maintenance, providing that it is followed by supporting integrated weight maintenance programmes in the follow-up period. This conclusion was confirmed by a meta-analysis of Ayyad and Andersen (2000), based on the literature from 1931 to 1999.

CHAPTER 6

Some metabolic consideration in relation to the use of VLCDs

6.1. Adaptation to (semi-) starvation and weight maintenance phase

Due to finely regulated metabolic adaptations, healthy subjects can sustain extended periods of total starvation without permanent harm (Owen et al., 1994). During the first 2-3 days of acute starvation, the major challenge to the organism is to provide carbohydrate in amounts sufficient to support the energy need of the brain (which cannot rely on fatty acids or protein oxidation). This is achieved by mobilization of hepatic glycogen stores (first 12-24 h) and is followed by stimulation of gluconeogenesis (24-72 h). However, this initial response is inadequate in the long term, because the glucose requirements of the brain (100-150 g/24 h) would demand the breakdown of 200-300 g protein/day, which exhausts rapidly the protein reserves of the organism. This problem is solved by a progressive increase in hepatic ketone body production, which tremendously increases the plasma concentrations of these substrates in the blood. Thus, ketone bodies become a preferential substrate for the brain, allowing a reduction of gluconeogenesis and hence a drop in net protein loss to ~30g/day. Subsequently, as starvation progresses, lean body mass (LBM) and consequently resting metabolic rate (RMR) decreases. It is known that the RMR slowly responds with the onset of energy deprivation. This was first documented by Benedict et al. (1919) during studies on caloric restriction in normal volunteers. In the Minnesota Experiment, in which 32 healthy men received 50% of their habitual intake (semi-starvation), Keys et al. (1950) demonstrated that RMR decreased during 24 weeks of semi-starvation. It is noteworthy, that at the end of the experiment there was no further change in RMR, indicating that a new equilibrium had been reached. This new energy balance is attained in part by a reduction in energy output, but also as a consequence of changes in body composition (Keys et al., 1950). Most of the recent experimental studies on the effects of energy restriction on energy metabolism have been performed in obese people. In short-term studies (few weeks) the administration of an energy reduction diet (300 - 1200 kcal/day) resulted in a decreased RMR (Cavallo et al., 1990; Fricker et al., 1991; Mathieson et al., 1986). Whether this fall in RMR is still significant related to fat-free mass (FFM) is unclear. Due to an intercept in the linear regression between FFM and RMR, the expression per kilogram FFM could lead to erroneous conclusions. Analysis of co-variance using FFM as the co-variate to adjust for body weight mostly does not show a significant reduction in RMR (Ravussin et al., 1989; Weinsier et al., 1992). In long-term studies (12-48 weeks) with obese subjects an absolute reduction in RMR has been found (Burgess, 1991; Donnelly et al., 1991; Foster et

al., 1990; Hammer et al., 1989; Wadden et al., 1990a). However, these reductions were no longer statistically significant when corrected for kg body weight or FFM in most of these studies (Donnelly et al., 1991; Foster et al., 1990; Hammer et al., 1989; Wadden et al., 1990a). Unfortunately, attempts to relate changes in energy expenditure to those in body composition are still prone to considerable error. Measurements of mean changes of FFM for a group of subjects may be relatively valid, but individual values are defaced by wide standard deviations (Waterlow, 1986).

Based on theoretical consideration, it is obvious that with a longer duration of energy restriction, the contribution of decreased FFM to the reduction in RMR increases (Shetty, 1990). This fall in RMR will be minimized (Garrow, 1986; 1987; Prentice et al., 1991). To obtain a more detailed answer, all the data of the experiments carried out between 1900 and 1990 have been set out with a meta-analysis (Melchionda et al., 1992). From this it was concluded, that variations of FFM caused by nutritional manipulations which modified weight are followed by corresponding modifications of RMR with a non-linear model, with a saving of FFM for large reductions of weight (Melchionda et al., 1992).

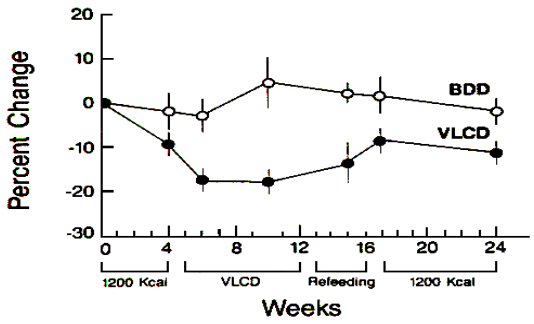
It appears that the principle determinant of RMR is FFM, or the proportion of mass that is muscle rather than fat (Kolata, 1987). Research suggests that exercise is effective in preventing a further decrease in RMR by maintaining or increasing FFM (Thompson et al., 1996). Exercise, especially weight training, causes hypertrophy, or increase in muscle size (Kreitzman, 1989). An increase in muscle mass is shown to increase RMR, or to counter decrease in RMR, because muscle tissue (FFM) uses much more energy than fat (Saris, 1996). As exercise increases fat oxidation, FFM is spared and further metabolic adjustment or decrease in RMR is not necessary (Whatley et al., 1994). Exercise is capable of offsetting the dietary adaptations of the body that result in decreased RMR (Donahoe, 1984). Exercise may restore RMR more quickly than diet alone by speeding up recovery of FFM (Saris, 1996). Moderate intensity exercise may prevent some decreases in RMR but does not return RMR to baseline (Thompson et al., 1996).

Weight loss is most rapid during the initial days of energy-restricted diet due to changes in sodium and water balance. The loss of water is a consequence of the breakdown of glycogen and protein, depending on the degree of calorie deficit and type of diet. Following this initial phase, weight loss will depend on the extent of energy deficit. With time, however, the rate of weight loss slows down again as the body's metabolic rate decreases and the energy deficit becomes smaller. The lower the energy content of the diet, the lower will be the metabolic rate due to higher weight loss. As a result, the rate of weight loss usually declines during the course of dieting (Prentice et al., 1991; Van Itallie and Yang, 1977).

After the period of hypocaloric feeding the resumption of normal energy intake causes an increase of the metabolic rate with a level significantly below that observed before the

beginning of the diet (Figure 6.1.). In this instance, the extent of decrease is proportional to the amount of weight loss (Foster et al., 1990). Nonetheless, an individual who has successfully lost weight will have significantly reduced total energy expenditure compared with before weight loss. This is not only due to a reduction in metabolic rate, but also to a reduction in the thermic effect of food (the individual eats less), and differences in physical activity (it takes less energy to perform the same amount of weight bearing activity for a smaller person). Thus, in order to maintain weight loss, individuals need to consume less energy than before dieting. These compensatory changes may account for the poor long-term efficacy of treatments for obesity (COMA, 1987; De Groot, 1988; De Groot et al., 1989; Leibel et al., 1995).

Figure 6.1. Percent change (± SEM) in RMR over a 24-wk study period in patients with a balanced-deficit (BDD, 1200 kcal/day) and a very low caloric diet (VLCD, 500 kcal/day)



[adapted from Foster et al., 1990]

When examining the results of different obesity treatments, it is tempting to use the "horse-race" method for evaluation. This approach primarily focuses on the question which treatment produces the greatest short- and long-term weight losses (e.g. LCD versus VLCD). Such an approach ignores the complexity of obesity (Foster and Kendall, 1994). There is a need for a better understanding of the underlying mechanisms, which include also hormonal changes during energy restriction.

6.2. Hormonal changes during acute energy restriction

During acute energy restriction (first 2-3 weeks) hormonal changes and subsequently substrate alterations occur to alter this adaptive component of the RMR. There are several hormonal systems which can be modulated by energy restriction. First, the sympathetic nervous system (SNS) and catecholamines, second, thyroid hormones, third, hormones related to glucose homeostasis and fourth, other calorigenic hormones. Furthermore, there is growing evidence that the human peptide leptin can be modulated by energy restriction and also plays a role in fertility. Changes in these hormonal systems may be responsible for the modulation of the cellular metabolic rate, substrate mobilization and fuel use (Danfort and Burger, 1989; Landsberg and Young, 1983; Shetty, 1990).

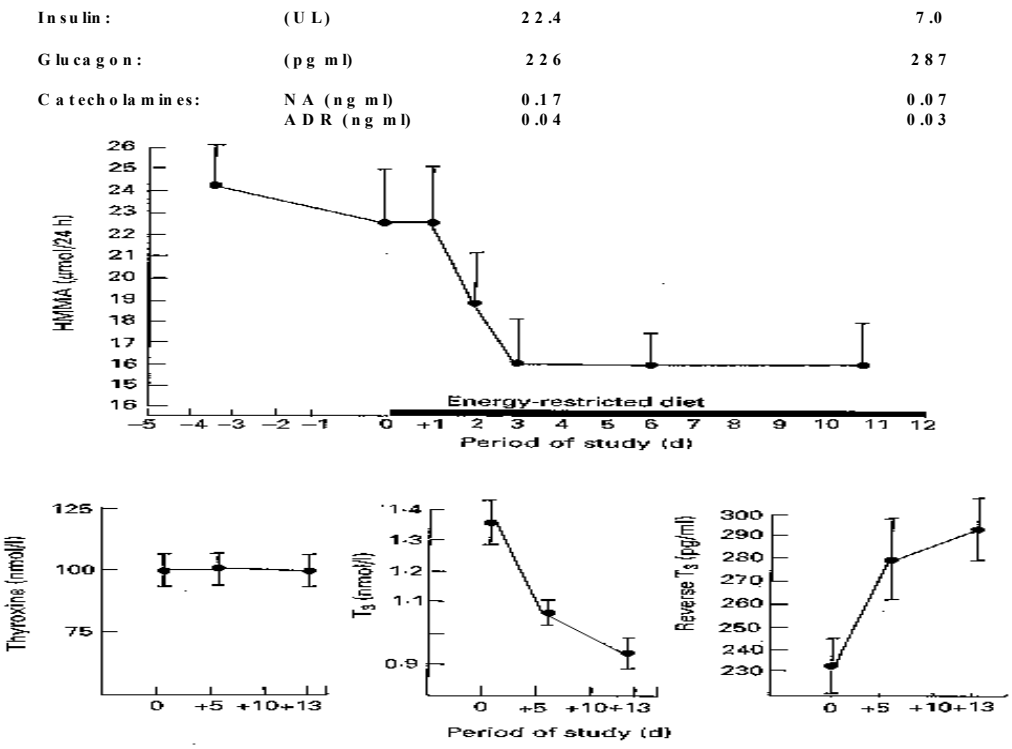
6.2.a. SNS and catecholamines

Stimulation of the SNS, and the concomitant release of noradrenaline and adrenaline, increases the metabolic rate of many tissues. The energetic actions of catecholamines are mediated by increasing the rate of cellular thermogenesis and by stimulating substrate mobilization. Changes in urinary levels of catecholamines can be consequences of altered rates of synthesis, release, turnover and excretion, and to any combination of these. Underfeeding generally results in reduction in both noradrenaline (NA) release and clearance rates such that the decrease of the plasma concentration of noradrenaline is minimal (O'Dea et al., 1982). Investigations in obese subjects have also shown that energy restriction is associated with a lowering in the circulating levels of noradrenaline along with a decrease in the urinary excretion of hydroxy-3-methoxymandelic acid (HMMA), a metabolite of catecholamines (Figure 6.2.).

6.2.b. Thyroid hormones

The thyroid hormones thyroxine (T4) and 3,5, -3'-triiodothyronine (T3) are very important in stimulating metabolic rate and thus play an important role in energy balance. A short-term very low caloric diet in obese people generally results in decreased T3 levels and unaltered T4 and TSH levels (Cavallo et al., 1990; Mathieson et al., 1986). There is also a rapid decline in serum T3 during fasting or partial energy restriction. The response of T3 to energy restriction seems to be most specific to restriction of carbohydrates (Hendler and Bonde, 1990; Hendler et al., 1986; Shetty, 1990). The decrease in T3 is rapid (within 24 h) and usually levels of 40-50 % below normal are reached within 3-4 days (cf. Figure 6.2.). Associated with the reduction in T3 there is an increase in reverse T3 (rT3) during fasting. After 2-3 weeks of fasting or semi-starvation the rT3 returns to normal levels at a time when the concentrations of T3 are being maintained at a low level. The reciprocal changes in T3 and rT3 concentrations during energy restrictions are bound to contribute to the reduction in metabolic rate, suggesting that the fall in T3 is an adaptive mechanism to conserve energy and preserve lean body mass (Osborne et al., 1983; Yang and Van Itallie, 1984).

Figure 6.2. Hormonal changes during acute semi-starvation in obese subjects



[Shetty et al., 1990]

Catecholamines influence the peripheral thyroid hormone metabolism. Adrenaline is known to enhance the peripheral conversion of T4 to T3 (Galton, 1965). On the other hand, thyroid hormones increase the number of β-adrenergic receptors in several tissues such as skeletal muscle and adipose tissue affecting the sensitivity of the peripheral tissue to catecholamines. These interactions between thyroid hormones and catecholamines may be the basis for their mutual role in the regulation of thermogenesis. Thyroid hormones are major regulators of RMR, while the regulation of adaptive thermogenesis is mediated largely by catecholamines. While administration of T3 even in low doses can prevent the drop in metabolic rate seen during energy restriction (Welle and Campbell, 1986), administration of catecholamines fails to stimulate metabolic heat production in hypothyroid rats. SNS-mediated thermogenesis in response to carbohydrate intake also requires thyroid hormones (Rothwell et al., 1982).

6.2.c. Hormones related to glucose homeostasis

Energy restriction influences glucose homeostasis. Low glucose and insulin concentrations (cf. Figure 6.2.) have often been monitored during periods of energy restriction (Atkinson and Kaiser, 1985; Escriva et al., 1992).

Insulin is the primary hormonal factor that controls the storage and metabolism of ingested metabolic fuels. After a meal, augmented insulin secretion facilitates the uptake and net storage of glucose, fat and protein. In skeletal muscle and in adipose tissue, insulin increases glucose transport, glucose oxidation and glycogen and protein synthesis, but inhibits proteolysis. In the liver, insulin inhibits gluconeogenesis, and very low density lipoprotein secretion. After an overnight fast, the decline in circulating insulin provides the stimulus for the mobilization of endogenous substrates, facilitating the production of glucose by the liver and the maintenance of glucose homeostasis. This reduction in plasma insulin levels is also bound to influence the RMR (Shetty, 1990). Insulin also stimulates the SNS by increasing catecholamine activity. Underfeeding abolishes glucose- and insulin-induced facultative thermogenesis (Christin et al., 1986; Gallen and Macdonald, 1990; Vollenweider et al., 1993). But the thermic effect of insulin per se is negligible in relation to the regulation of energy balance in obese subjects. Short-term weight loss by VLCD induced a significant decrease of FFM with a concomitant decline of absolute RMR values. A non-significant decreasing trend exists for thermogenesis. No further decrease of FFM was found after long-term weight loss without differences in RMR/FFM or thermogenesis (Van Gaal et al., 1992).

Glucagon, a hormone that is secreted when the blood glucose concentration falls, has several functions, which are diametrically opposed to those of insulin. Stimulated glycogenolysis and increased blood glucose concentration are the most important effects of glucagon. These reciprocal changes in pancreatic peptide hormones are generally considered to be an essential adaptive mechanism aimed at maintaining glucose production during the first days of starvation. With prolongation of the fasting, plasma glucagon levels return towards basal values due to a reduction in secretion and a progressive decline in metabolic clearance. The increased glucagon secretion associated with the insulin deficiency in the early phase of energy restriction may contribute little to increase the metabolic rate (Shetty, 1990).

6.2.d. Other calorigenic hormones

Other hormones with potential metabolic and calorigenic activity, such as growth hormone and leptin, also change rapidly during the early phase of total starvation or semi-starvation.

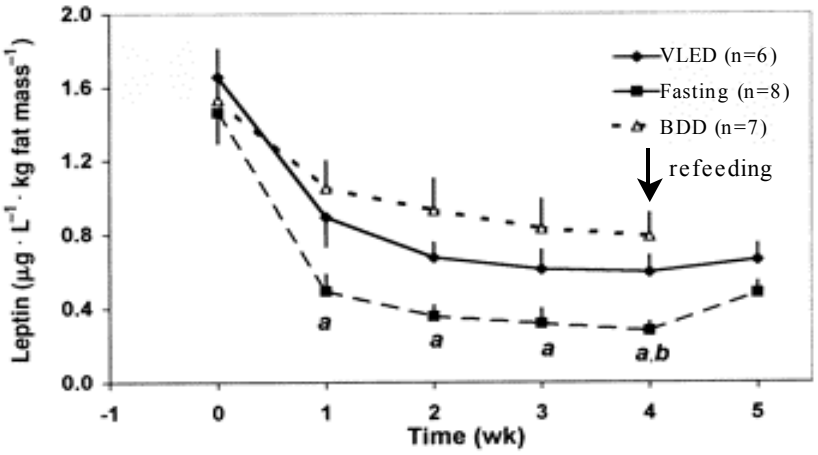
Growth hormone (GH) is also thermogenic and is known to produce a small but significant effect on the RMR. GH is described as having anabolic, lipolytic and insulin antagonist properties which probably serve to promote optimal substrate utilization during periods of energy restriction (Shetty, 1990; Vance et al., 1992).

Leptin is a 167-amino acid peptide produced mainly in adipose tissue. Its absence produces the obese (ob/ob) mouse, which is characterized by obesity, hyperphagia, hyperglycaemia, hyperinsulinemia and insulin resistance. Leptin corrects these defects (Bray and York, 1997; Friedman, 1998). Plasma leptin concentrations are higher in obese humans than in lean and are rapidly decreased by initial weight loss (1000 kilocalories/day). There is no evidence that baseline leptin concentration or the changes in leptin, which accompany initial weight loss, are predictive of subsequent weight regain (Wing et al., 1996; Torgerson et al., 1999). There was a trend for a greater decline in leptin with greater energy deficit.

The fall in plasma leptin was greatest in the fasting group and intermediate in the VLCD group (Figure 6.3.)(Wisse et al., 1999). The change in leptin per kilogram fat mass correlated in this study with glucose concentration but not with fat mass. During refeeding postfasting, leptin increased, despite an ongoing loss of fat mass and correlated positively with changes in resting energy expenditure. These results support the premise that insulin-mediated glucose uptake by adipocytes primarily modulates leptin concentration. Furthermore, after a fast, refeeding a diet providing energy intakes considerably below requirements increases leptin concentrations and energy expenditure even with ongoing fat mobilization.

In contrast to other hormones, leptin might be of minor importance for the neuroendocrine response to energy restriction in obese humans (Torgerson et al., 1999). Recent research shows that leptin injection has no effect on weight loss, energy metabolism and the SNS in obese subjects (Hukshorn et al., 2000). It does appear to have an effect on hunger/satiety, which might be beneficial for the compliance of subjects to the diet. This was confirmed recently in a RCT with leptin/placebo injection during a VLCD diet. Subjects receiving leptin injection lost significantly more weight (Hukshorn et al., 2001). Based on these results it is suggested that perhaps the absence of leptin during energy restriction triggers adaptive responses such as reduction in RMR, SNS activity and reproductive functions (Hileman et al., 2000).

Figure 6.3. Effect of prolonged moderate and severe energy restriction and refeeding on plasma leptin concentrations in obese women

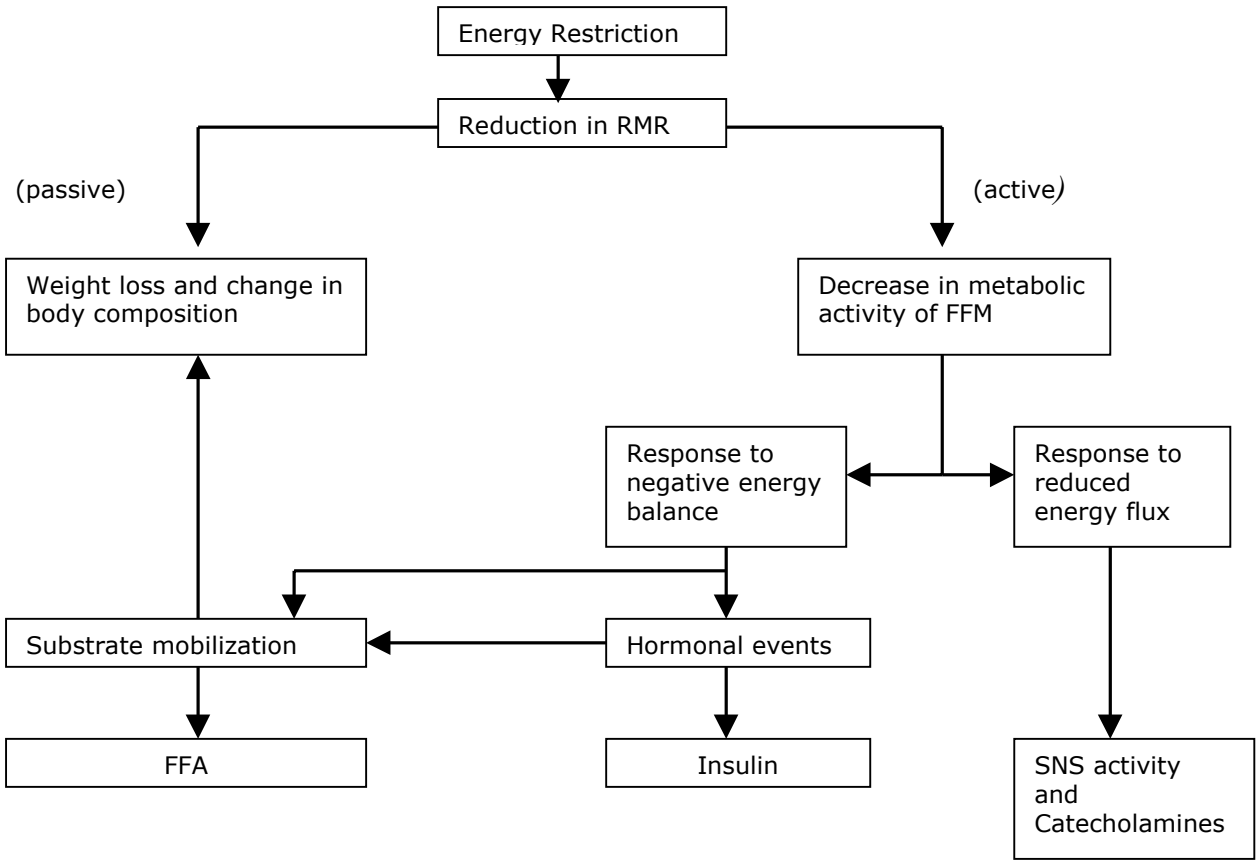


Very Low Energy Diet (VLED), Low-Energy, Balanced-Deficit Diet (BDD)
a significantly different from BDD, $p<0.001$
b significantly different from VLED, $p=0.005$

[adapted from Wisse et al., 1999]

Figure 6.4. summarizes the possible mechanisms involved in the adaptive reduction in RMR during short-term energy restriction. Over a short period, the decrease in metabolic activity of the body tissues primarily contributes to this reduction. In the long run the loss of body tissue contributes more to the lowered RMR. Several physiological mechanisms, chiefly hormonal, operate to decrease the metabolic activity of the tissue mass to enhance its metabolic efficiency. SNS activity is toned down, signalled by the decrease in energy flux, while the negative energy deficit initiates changes in peripheral thyroid metabolism and lowers insulin secretion. The reductions in the activities of these three key thermogenic hormones probably act in a concerted manner to lower cellular metabolic rate. Changes in other hormones such as glucagon and growth hormone will influence these alterations. In association with the insulin deficiency these changes will promote endogenous substrate mobilization which in turn leads to an increase in circulating free fatty acids (FFA) and ketone bodies. The elevated FFA, alterations in substrate recycling and protein catabolism will also influence the resting energy expenditure (Shetty, 1990).

Figure 6.4. Possible mechanisms involved in the adaptive reduction in resting metabolic rate (RMR) during short-term energy-restriction



[adapted from Shetty et al., 1990]

6.3. Nitrogen balance during VLCD use

The metabolic response to VLCD involves, among other things, a gradual decline in gluconeogenesis accompanied by an increasing reliance on fat-derived fuels that limits the loss of body protein. In adults VLCDs frequently provide daily protein intakes below the recommended dietary allowance (RDA) of 0.8 g/kg, despite evidence that calorie restriction increases the protein requirement for zero nitrogen balance (Committee on Dietary Allowances, 1980; Calloway, 1975). The relative efficiency of the substrates protein and carbohydrate to spare lean tissue during energy restricted diets has been the

subject of considerably controversy (Apfelbaum et al., 1970; Blackburn et al., 1973; Aoki et al., 1975; Baird et al., 1974; Greenberg et al., 1976; Genuth et al., 1974; Bistrian et al., 1977; Marliss et al., 1978; Howard et al., 1978; De Haven et al., 1980).
This section focuses on the question: what is the relative amount of protein and carbohydrate needed in these diets for protein sparing. Zero nitrogen balance during energy restriction is not physiological since the acceptable weight loss composition of 75% fat mass and 25% fat-free mass automatically leads to a moderate negative nitrogen balance. The primary focus is therefore to avoid excessive nitrogen loss.

Studies of protein sparing during weight reduction in obese individuals with VLCDs have shown conflicting results; nitrogen balance studies have been carried out following differently formulated VLCDs providing different amounts of protein and/or carbohydrate, have been relatively short-term (five to ten days) and have been criticized for their failure to take into account stool and integumental losses of nitrogen. Moreover, most studies were uncontrolled (Yang and Van Itallie, 1976; Fisler and Drenick, 1987; Pasquali et al., 1987; Hendler and Bonde, 1988; Gelfand and Hendler, 1989; Vazquez and Adibi, 1992).
In a controlled study (De Haven et al., 1980), seven obese individuals, ranging in age from 23 to 38 years and weighing between 120 and 169 kg (mean 141 kg, 80 to 120 per cent above their ideal body weight) followed sequential 400 kilocalories diets providing either 100 g protein alone, or an isocaloric mixture of 50 g protein and 50 g carbohydrate three to five weeks for each diet. Mean daily negative nitrogen balance in subjects receiving the mixed diet was not significantly different from that observed after the pure protein diet. With both diets nitrogen balance was more negative during the first week than during the last week. However, the responses during the first or last week were not significantly different with the two diets. To determine whether protein diets result in better nitrogen balance if given for more prolonged periods, each diet was given for a 5 and half -week period. Beyond three weeks in which the net nitrogen losses were comparable between the two diets, nitrogen balance became zero after four to five weeks of each diet regimen. These data indicate that zero nitrogen balance can be achieved with both diets and that concentrated protein diets offer no nitrogen-sparing advantage as compared with isocaloric mixed carbohydrate-protein diets.

Vazquez et al. (1995) assessed the independent effects of carbohydrate and protein intakes in protein sparing during a VLCD. Forty-eight obese women were randomly assigned to consume isoenergetic (600 kilocalories) liquid diets that provided the following amounts (g/d) of protein and carbohydrate, respectively, for 28 days: 50 and 10, 50 and 76, 70 and 10, and 70 and 86. Cumulative nitrogen losses were lower in the high carbohydrate groups than in the low carbohydrate groups, but were similar in the groups receiving 50 and 70 g protein/day. By day 28, the subjects in the 70 protein/86 carbohydrate group were in positive nitrogen balance, while nitrogen balance was negative, albeit in near equilibrium in the other VLCD groups. Thus, VLCDs that provide 70 g protein/day are not superior to those providing 50 g protein/day for protein sparing

during weight reduction regardless of whether they contain high or low amounts of carbohydrate. Furthermore, a higher carbohydrate intake in an isocaloric VLCD results in sparing of lean body mass in 28 days, depending on the protein content of the VLCD. Taken together, the total carbohydrate and protein intakes are both important for protein sparing during weight reduction; the effects of the carbohydrate and protein content of the VLCDs are additive.

Bistrian et al. (1981) assessed rates of total body protein synthesis, breakdown and amino nitrogen flux in five obese young adult women who were fed a mixed diet of 0.8 g meat protein and 0.7 g carbohydrate/kg ideal BW and approximately 450 kilocalories, for 3 weeks. Nitrogen balance remained significantly negative during each week of the mixed diet and was overall negative (-3.3 ± 0.9 N/day); amino nitrogen flux, total body protein synthesis, and breakdown values fell significantly by the third week. It was concluded that total body protein synthesis and the net balance between synthesis and catabolism can not be maintained with this diet during this short period of three weeks.

Wechsler et al. (1984) studied 61 obese patients, randomized into four groups, with modified fasting providing 240-450 kilocalories/day; the daily diet consisted of 33-55 g protein/day, 1-10 g fat/day and 25-45 g carbohydrates/day. In contrast to the other studies with restricted protein intake, the nitrogen balances could be equilibrated from the third week on.

Koppeschaar et al. (1983) studied 18 obese subjects (relative weights 131-205 per cent) for 28 days during a very low calorie diet, composed of 50 g protein and 50 g carbohydrate. Nitrogen balance was attained from the fourth week onwards.

Wilson and Lamberts (1979) found in a study in eleven obese patients receiving a liquid formula diet for a period of 4 weeks containing 320 kilocalories, 31 g protein, 44 g oligosaccharides, and 1.5 g fat that nitrogen balance remained slightly negative, with a mean daily deficit being 1.3 g N/day at the end of the study.

Based on the available literature it can be concluded that with an intake of 50 g protein per day of high biological value, undesirable levels of lean tissue breakdown and consequently unacceptable negative nitrogen balances can be avoided. The level of carbohydrate intake has a positive effect on the nitrogen breakdown. Levels up to 40-45 g carbohydrate per day do have a protein sparing effect.

6.4. Ketosis and protein catabolism during VLCD

Since the original report published by Sherwin et al. (1975), indicating a decline in circulating alanine levels and in protein catabolism in subjects infused with ketone bodies, the concept has emerged that an enhancement in ketogenesis attending total fast, and to a lesser extent the semi-starvation (”protein-supplemented fast”) may exert a protein sparing effect. This assumption was also based on the concomitant moderate rise in ketonaemia and reduction in nitrogen loss occurring after the first week of severe reduction in energy intake (Kolanowski et al., 1983; Gougeon et al., 1992). Further studies did not confirm, however this postulated inhibitory influence of ketones on protein

catabolism in man (Miles et al., 1983; Vazquez and Adibi, 1992; Vazquez and Kazi, 1994), and the question whether ketones may really spare body proteins during caloric deprivation became the subject of considerable controversy. As to the reduction in net loss of protein, which is usually seen after several weeks of very low calorie diets, concomitantly with a mild ketosis, it has been even suggested that this apparent sparing of protein is solely due to the increased rate of protein synthesis occurring in face of unchanged protein breakdown (Halliday et al., 1993).

Moreover, the results of several studies clearly indicate that, aside from a sufficient intake of high quality proteins, the protein-sparing effect of VLCD is related essentially to the amount of carbohydrates provided in the diet, which exert at the same time an anti-ketogenic effect (Gougeon et al., 1992; Vazquez and Adibi, 1992). This concept was considerably reinforced by the studies of Vazquez and coworkers (Vazquez and Adibi, 1992; Vazquez and Kazi, 1994), clearly indicating that in response to VLCDs allowing similar energy and protein intake, the protein oxidation was even higher and the nitrogen balance more negative during ketogenic (low carbohydrate) than non-ketogenic (high carbohydrate) very low calorie diet.

The ketogenic formula of VLCD should therefore be no more advocated in an attempt to reduce the loss of body proteins during severe energy deprivation, the protein-sparing properties of VLCD depending essentially on sufficient intake of carbohydrate and of high biological quality of ingested proteins.

6.5. Ketosis and calcium balance during VLCD

Contrasting with the renal loss of calcium during total starvation (Stein et al., 1983), which results apparently from the fast-induced acidosis increasing calcium release from bone and reducing tubular calcium reabsorption (Stein et al., 1983; Grinspoon et al., 1995), the urinary excretion of calcium remains unchanged in subjects undergoing VLCD-treatment. While anorexia nervosa or a chronic poor nutrition seen in obese subjects after gastro-intestinal surgery are associated with negative calcium balance, bone mass loss, and increased fracture risk, little is known about the short-term effects of VLCD on bone mass. In a study published by Compston (1993), the total body bone mineral content (BMC), as well as total body bone mineral density (BMD) were significantly reduced after 11 weeks of VLCD, the magnitude of this effect being correlated to the degree of reduction in body weight, as well as in fat and lean mass. During the subsequent regain of weight the baseline BMC and BMD were nearly completely restored (Compston, 1993). This study did not provide information whether the diet-induced bone loss persists when weight loss is maintained after dieting.

The results of a more recent study (Andersen et al., 1997) suggest that increasing the energy content of very low calorie diets to 925 kcal/day may prevent the reduction of total BMD and BMC, but not the mineral loss from the femoral neck and greater trochanter. Diet

plus resistance training was not associated with a significantly better outcome on either of these measures versus diet alone (Andersen et al., 1997).

While Nishizawa et al. (1992) reported that serum ionized calcium, as well as total serum calcium, plasma PTH and calcitonin levels remain stable even during the 4-week long VLCD, Davie et al. (1986) reported that calcium balance may be positive in obese subjects undergoing a moderate VLCD (780 kcal/day) providing a high calcium intake (averaging in this study 1200 mg/day), and that the retention of ingested calcium is proportional to the amount of carbohydrate in the diet (Davie et al., 1986).

These rather reassuring observations do not allow however, the conclusion that bone mineral content could not be affected during VLCD, even if it lasts for several weeks. Indeed it has been recently reported that bone mineral density, which is usually increased in obese subjects, is slightly but significantly reduced after 1 year of severe reduction of energy intake (800 kcal per day during the first 3 months followed by a 1000 kcal diet) inducing a 17% reduction in the initial body weight (Gossain et al., 1999). Nevertheless, despite this moderate reduction in the bone mineral content, the bone mineral density remained within normal range in these subjects, even after 1 year of dieting.

Taken together, all these observations raise some concern about the risk of a moderate loss of bone mineral content during VLCD. To prevent such a consequence of dieting, the VLCD should provide a sufficiently high intake of calcium and vitamin D, as well as an appropriate amount of carbohydrate.

6.6. Ketosis and hyperuricaemia during VLCD

While a prolonged but moderate reduction in energy intake induces a significant reduction of hyperuricaemia and in the frequency of gouty attacks in overweight patients with gout (Dessein et al., 2000), the VLCD is usually associated with a moderate (20 to 30 %) increase in serum uric acid levels. However, the exacerbation of gout during VLCD, albeit reported (Atkinson, 1990; Atkinson and Kaiser, 1981), remains exceptional (since it occurs in no more than 1% of patients undergoing VLCD), and this risk exists essentially in patients with previous history of gout. According to Kolanowski et al. (1983), serum uric acid increased after 10 days of VLCD (420 kilocalories/day) from 6.06 ± 0.49 to 7.74 ± 0.52 mg/dl ($p<0.01$), concomitantly with a moderate increase in ketonaemia (plasma 3OH-butyrate levels increasing from 0.24 ± 0.09 to 1.08 ± 0.37 mM, $p<0.001$). Despite this rise in serum uric acid concentration the urinary urate excretion decreased slightly (n.s.), from 431 ± 86 mg/24 hours before to 351 ± 87 mg/24 hours on day 10 of diet, indicating a clear-cut reduction in renal urate clearance. However, the enhancement in protein catabolism rather than ketosis represented a main mechanism of hyperuricaemia attending the severe energy-restricted diet (Gougeon et al., 1992), and the rise in uricaemia may be completely prevented by allopurinol administration (allopurinol is a xanthine oxidase inhibitor and as a result its administration leads to a lower uric acid

production). That the VLCD-induced hyperuricaemia is induced by (nucleo)protein catabolism rather than by ketosis as such, is strongly suggested by the fact that after 10 days of VLCD, both protein catabolism and serum uric acid levels fall progressively despite persistent ketonaemia (Gougeon et al., 1992). In addition, when ketonaemia similar to that induced by VLCD are reproduced by 3OH-butyrate infusion in normal subjects, serum uric acid levels remained unchanged. Indeed, in the latter study subjects received during 3 hours the D(-)3OH-butyrate infusion at a rate of 20 µmol/kg/min increasing plasma 3OH-butyrate levels to 1.5 mM. Despite this rise in ketonaemia, plasma urate levels were unaffected, averaging 4.49 ± 0.46 mg/dl before and 4.44 ± 0.46 mg/dl at the end of 3OH-butyrate infusion, and there was no change in urinary urate handling.

It may be therefore concluded that a moderate hyperuricaemia which occurs in patients submitted to VLCD is a transient phenomenon, occurring during the first 10 to 14 days of this severe energy restriction, as a result of an enhancement in protein catabolism. The risk of gout attack is very low, and exists probably only in subjects already suffering from gout. The increase in serum uric acid levels is unrelated to ketosis, and may occur as well during 'ketogenic' as 'non-ketogenic' VLCD.

CHAPTER 7

SAFETY ASPECTS OF VLCD*

7.1. An overall appraisal of safety of VLCD as determined by published studies over the years 1929 to 2000

The consideration of the safety of VLCD has been deliberately restricted to information relating to VLCDs as defined in this report (Chapter 2). This definition excludes both the liquid protein diets which have not been available for at least the past 20 years, or other very low energy diets which are not nutritionally complete. These preparations should not be used as the sole source of nutrition and are excluded by the definition.

Over 460 studies covering over 52,000 dieters were identified in the scientific and medical literature between 1929 and 2000. These studies cover a very substantial number of different VLCD formulae, all, by definition, having a daily intake under 800 kcal. Their composition was regarded by those undertaking the studies as containing adequate levels of macronutrients and micronutrients. The vast majority of these studies were published in the period from 1986 to 2000 (representing some 47,000 dieters).

Studies were only included in the current analysis if they contained prime data (Table 7.1.). These data embrace a wide range of composition, energy content and length of use (Table 7.1.). In addition to these identifiable data there has been free-sale use in several countries for periods up to 20 years covering well over 20 million dieters (Marks and Schrijver, 2001). Examination of the scientific literature, records or publications in the public domain has disclosed no fatal adverse event which can be attributed to the use of VLCD.

The papers until about 1995 provided clear information on side effects and adverse reactions. These indicate that in those who are healthy apart from their excess weight, side effects are a nuisance rather than a serious problem or life threatening. Only occasionally do they lead to the diet being discontinued.

*In addition to the information in the consulted documents (Section 1.4.), analyses and appraisals of the recent studies undertaken on VLCD including some unpublished material were made available to the Committee. This material has been consolidated and is available as a Report from the VLCD European Industry Group. See section 1.4. Only the reference within this chapter are to be found in the bibliography to this Report.

Table 7.1. The prime clinical and experimental data on VLCD

		no. of studies	%	no. of subjects	%
Energy/day	< 400 kcal	111	27.4	4182	9.1
	400-599 kcal	261	64.4	40674	88.6
	600-799 kcal	33	8.1	1053	2.3
Protein/day	< 50 g	180	43.6	19212	38.0
	> 50 g	233	56.4	31303	62.0
Carbohydrate/day	30-40 g	149	44.2	34194	80.4
	41-45g	81	24.0	3922	9.2
	46-50g	25	7.4	763	1.8
	>50g	82	24.3	3627	8.5
Length of use	< 4 weeks	81	17.9	17006	32.9
	4 weeks and more	371	82.1	34705	67.1

Note: the total number of studies and subjects varies because not all studies provided full information.

In those who are receiving medication, for example for diabetes and hypertension there is a need to adjust dosage. There are relatively few studies of the side effects of formula diets in the range 800–1200 kcal. Only Rössner and Flaten (1997) conducted a RCT comparing VLCD and LCD on side effects. The LCD group tended to report fewer adverse effects although this did not result in a significantly higher compliance. Also weight loss was similar in the VLCD and LCD groups. It is therefore not possible to give a reliable indication of the comparative incidence of side effects between LCD and VLCD at equivalent levels and rates of weight reduction. The overall impression is that these are similar.

The current lack of concern about side effects in the medical press is indicated by the absence of any reference to side effects in most publications since about 1995. Table 7.2. records the side effects, the mechanism and method of control.

A realistic appraisal of the incidence of side effects is provided by the paper by Kirschner et al. (1988). This study involved 4026 dieters over some 40,000 weeks of dieting. They were using a VLCD containing 420 kcal/d and some 10% of the dieters was in the BMI range <30 kg/m^2. The most common problems noted were early postural light headedness and tiredness. The most common late complaint was that of mild transient hair loss. In Table 7.3. the severe adverse events observed in this large cohort are tabulated.

Table 7.2. Side effects, their possible mechanisms and appropriate management

SIDE EFFECT	MECHANISM	MANAGEMENT
Dry mouth/halitosis	dehydration due to diuresis, ketosis	increase fluid intake
Diarrhoea	concentrated minerals lactose intolerance	split into several more dilute meals lactase pre-treatment
Constipation	low bulk	increase fluid intake and give non-digestible bulking agent
Headache	dehydration	increase fluid intake, mild analgesics
Nausea/vomiting	concentrated minerals	increase fluid intake
Dizziness/ orthostatic hypotension	dehydration	increase fluid intake
Cramps/ fatigue	dehydration/shift of muscle glycogen/fluid	increase fluid intake, stops as weight stabilizes
Hunger	low bulk/subject may be non-ketotic	split diet into more meals/check about snacking
Visual disturbance	dehydration	increase fluid intake; rapidly clears
Feeling cold	reduced metabolism and subcutaneous fat	only temporary problem/advise warming measures/corrects naturally
Hair thinning	modification of hair cycle	hair grows back well as weight stabilizes*
Skinfolds	lost weight	corrects naturally*
Irregular menses (rare)	steroid release	corrects naturally*
Gallstones (rare)	stasis in gallbladder/supersaturated bile	ensure VLCD provides 7 g or more fat/day
Gout (rare)	uric acid rise	give allopurinol

*adaptive response [adapted from Marks and Howard, 1997]

Table 7.3. Severe adverse events observed in patients on VLCD

	CASES
- acute gout	8
- foot drop (temporary)	2
- acute psychosis	4
- diabetic ketoacidosis	2
- late hair loss	10 %
- cardiac arrhythmias	
supraventricular tachycardia (hypoglycemia)	1
multifocal PVCs	2

[data from Kirschner et al., 1988]

In view of the great concern regarding cardiac arrhythmias in patients on VLCDs the literature was carefully screened for such occurrences. Over the 8-year period, only one patient was documented who developed a supraventricular tachycardia clearly related to hypoglycemia and corrected with intravenous glucose supplementation. Two patients required hospitalization for the development of palpitations associated with multifocal PVCs (premature ventricular contractions) (Kirschner et al., 1988).

Non-complications

In view of the concern as to the overall safety of VLCDs there were several important non-complications to record in the study of Kirschner et., 1988), including: (1) coronary bypass surgery without complications in eight patients; (2) major breast surgery without complications in twelve patients; (3) pregnancies occurring while patients were on VLCD (without subsequent complications) in six women in whom the diet was subsequently discontinued.

In addition to these general side effects, special attention has been paid to data relating to concerns about severe adverse reactions that have been expressed in earlier original papers and review articles and discussed in the SCOOP working group, based on the earlier fatal cases using the so-called liquid protein diet (FDA, 1979a; 1979b; Isner et al., 1979; Sours et al., 1981; Van Itallie et al., 1984).

Based upon a review of the existing original reports and data, the following observations and conclusions can be drawn:

- While the exact cause of the cases of syncope and sudden death occurring with liquid protein diets was not established, it is apparent that all those that were studied (17 cases) took place after over 2 months use of formula foods (median 5 months), mostly with poor amino acid profiles and suspect vitamin/mineral content. Two patients used regimens with high quality protein and two supplemented the low quality liquid protein with food protein of high quality (Federal Register, 1980; Sours et al., 1981); some took calcium supplements (Felig, 1984). Many were under direct medical practitioner control, with ECG and blood biochemical monitoring which had not indicated a problem.
- There is record of prolonged use of nutrient complete VLCD both in trials and free sale for about two decades. So far the reported serious adverse events are minimal especially in the light of the increased prevalence of co-morbidities related to obesity. In particular the arrhythmias produced with the liquid protein regimens are not observed with the higher quality VLCDs when examined prospectively (Felig, 1984).
- There is no clinical evidence nor are there laboratory studies of specific adverse effects attributable to the use of VLCDs on any organ, including heart, kidney or liver. Several studies using VLCDs have shown improvement in disorders associated with excess weight (e.g. hypertension, type II diabetes mellitus, sleep apnoea syndrome) (Kirschner et al., 1988; Mustajoki and Pekkarinen, 2001).
- Several studies have examined the effect of VLCD on the electrocardiogram (i.e. both regular single observations and continuous Holter monitoring) and these have shown no evidence of alteration of cardiac function, other than that already present in a number of untreated obese subjects (Carella et al., 1996), or leads to improvement (Alpert et al., 2001). Unfortunately these data are not as valuable as it might appear because the period of Holter monitoring is generally shorter than the time when abnormalities were encountered with liquid protein diets (Marks and Schrijver, 2001).
- It has been suggested that the rapid loss of weight produced by VLCD increases the risk of cholelithiasis. The data presented (Festi et al., 1998; Marks and Schrijver, 2001) indicate that cholelithiasis was most probably related to the low fat content of commercial versions of VLCD used in the early days in the USA. A higher incidence of cholelithiasis has not been noted in Europe and this is probably related to the higher fat content (minimum about 7 g) in VLCD used in Europe. This was also corrected when higher levels of fat were included in the American VLCD diets. An alternative approach in the USA has been the use of one meal each day containing 5 g fat. Cholelithiasis is a recognized problem in obesity and is increased with all forms of weight loss. Studies indicate that this risk is not limited to VLCD (Spirt et al., 1995; see also Section 5.6.). A minimum daily fat content of 7 g, which also provides for the essential fatty acid requirements, is considered as sufficient.

- In the older literature there are suggestions that dieting, and particularly that with VLCD can lead to eating disorders (anorexia nervosa, but particularly bulimia). Recent papers point out that by the very nature of the disorder it would be anticipated that there would be an association with dieting, since disturbed body image appears to be a factor in the genesis of these psychiatric diseases. However there is no evidence in either adolescents (Smolak and Levine, 1994; Gustafson-Larson and Terry, 1996) or in adults (La Porte, 1992; Wadden et al., 1994; National Task Force, 2000) that dieting is causative. Furthermore, there is no evidence that use of VLCD specifically increased the risk of eating disorders.

7.2. Examination of the reputed problems with the use of VLCD

7.2.a. VLCD and Resting Metabolic Rate

It has been suggested in the earlier literature that the use of VLCD (as opposed to LCD) substantially reduces the RMR and in consequence that there is a greater subsequent difficulty in avoiding weight increase after VLCD have been used. This has been re-examined in several recent studies (Coxon et al., 1992; Van Gaal et al., 1992; Kreitzman et al., 1993; Apfelbaum, 1993; Marks and Schrijver, 2001 via VLCD Industry Group).

- There is an initial and temporary (about 10-14 days) physiological reduction in RMR of about 15% due to the lower intake of food. The level of reduction is depending on the level of energy deficit. The reduction may be more rapid with VLCD than LCD for the first few days of dieting. This is thyroid mediated and beneficial since it spares protein at this stage (see Section 6.2.).
- Even if the RMR is lower, this has no clinical relevance to the weight-reducing effect of the diet because the weight loss is dependent on the total energy use and not the RMR (Van Gaal et al., 1992; Wadden et al., 1992; Kreitzman et al., 1993). Subsequently, once weight stability is achieved, the RMR is dependent on the actual weight of the dieter and in particular the actual FFM (James et al., 1978; Kreitzman et al., 1993) (see Section 6.1.).

7.2.b. Relationship between energy deficit and rate of weight loss

Based on the energy deficit, a certain rate of weight loss can be expected. Compliant use of VLCD will produce a more rapid loss of weight and a greater total weight loss than LCD. However, available RCTs comparing VLCD and LCD do not show substantial greater weight losses. This is most probably related to the compliance (Saris, 2001).

Studies that have achieved good compliance demonstrate that the greater the energy deficit between the diet and the total energy expenditure (Kreitzman et al., 1993) the more rapid is the weight loss. On a study population basis there is surprisingly good agreement with the theoretical relationship on the basis of the weight loss being approximately 75 % fat / 25 % fat free mass (COMA, 1987; Muller and Grossklaus, 1993)

that 1 kg weight loss corresponds to an energy deficit of about 7000 kcal. A comparison of the average weight loss achieved with compliance on various methods is shown in Table 7.4.

Table 7.4. Average weight loss per week with various energy deficits, based on 4-8 weeks dieting

Weight loss procedure	Average loss per week (women)	Reference
1200 kcal diet daily	0.3-0.7 kg/week	Heshka et al., 1996: Toubro and Astrup, 1997; Wadden, 1993
800 kcal diet daily	0.7-1.4 kg/week	Davies et al., 1989; Garrow, 1993; Hill et al., 1987
300-500 kcal diet daily	1.5-2.5 kg/week	Hoie and Bruusgaard, 1995; Pekkarinen et al., 1996; Ryde et al., 1993a; Ryttig et al., 1997; Toubro and Astrup, 1997; Wadden, 1993

7.2.c. Weight fluctuation (weight cycling; yo-yo effect)

As a result of some earlier studies it is suggested that VLCD increased the yo-yo effect and that this weight cycling is medically undesirable. Weight fluctuation is in itself psychologically undesirable, because it is depressing for the dieter. However, data are lacking that this is related to the use of VLCD.

Weight fluctuation is a feature of dieting in general. Recent studies have indicated that cycling does not have an adverse effect on body composition (Forbes, 1987; Van Dale and Saris, 1989; Prentice et al., 1990). Hence the metabolic rate and the rate of weight loss of the various cycles are equivalent. Nor does weight fluctuation have any inherent medical dangers (e.g. no excess central fat deposition or loss of muscle mass)(Van Dale and Saris, 1989; Wadden et al., 1992; Kamrath et al., 1992; Van de Kooy et al., 1993). The rate at which weight regain takes place during a maintenance phase depends on the difference between the energy intake and the reduced energy requirements inherent to the lower FFM, not on the energy level of the diet used to achieve the weight loss (Weinsier et al., 2000).

7.2.d. The safety of continuous use of VLCD as opposed to intermittent short periods

There is now adequate experience to demonstrate that from the safety point of view, continuous administration for longer than two to three months to the target weight is at least as safe as intermittent use with intervening periods of a higher energy intake (Kreitzman and Beeson, 1996, Pekkarinen and Mustajoki, 1997; Rössner, 1998; Mustajoki

and Pekkarinen, 2001). From the point of view of ease of use the continuous procedure has been shown to be preferable.

7.3. Analysis of the reputed extra risk in treating dieters at BMI between 25 and 30 kg/m^2 as opposed to those who have a greater body mass index

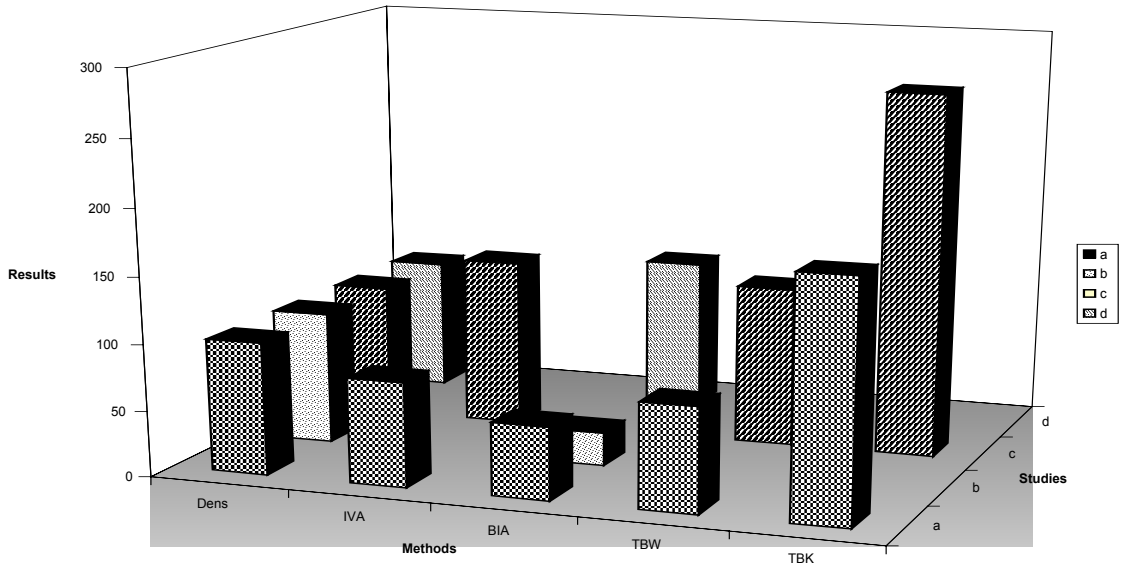
Since 1987 it has been held that loss of weight in those who have a greater fat content results in a lower proportional loss of the associated protein than in those with less excess fat (Forbes, 1987). From this it has been assumed that there is a greater health risk in slimming in the overweight than in the obese. This was further extended to an assertion that VLCD should not be used below a BMI of 30 kg/m^2. Examination of the literature on weight reduction and particularly the numerous reviews that have appeared over the years demonstrates that this view stems from the experimental work of Forbes in the late 70s and early 80s and of a review on this issue by Prentice et al. (1991).

From a theoretical point of view based on the second law of thermodynamics, negative energy balance will lead to higher proportional loss of lean body mass in lean versus obese subjects due to the lack of available energy from the fat stores. However, the question remains at which level of energy deficit and at which level of body fatness or leanness, the associated protein loss exceeds the accepted 75/25 ratio level FM/FFM loss.

An examination was therefore undertaken to analyze this concept. A review of the body composition data relating to weight loss at various BMI levels disclosed a total of about 100 apparently relevant studies which have been found in a literature search from 1960 to 2000. Of these 67 have been subjected to careful appraisal and reanalysis. These 67 studies include all the 41 papers used by Forbes and Prentice et al.

As part of this study, the reliability and reproducibility of the many different indirect methods of estimation of body composition were subjected to critical appraisal (Figure 7.1.).

Figure 7.1. Comparison of the body composition results found using five different methods in four different studies. Densitometry results are taken as 100 and the results of the other methods compared.



Methods: Dens: Body Densitometry
IVA: Infrased interactance
BIA: Bio impedance
TBW: Total body water
TBK: Total Body Potassium

a: Ryde et al., 1993b
b: Deurenberg et al., 1989
c: Albu et al., 1992
d: Valtuena et al., 1995

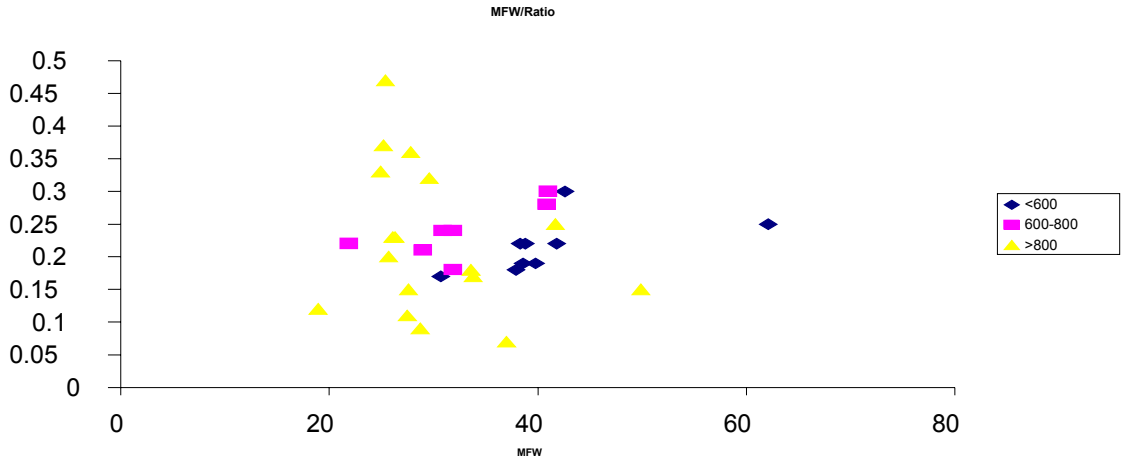
[Based on data in Marks and Schrijver, 2001]

It became obvious that part of the Forbes conclusions stemmed from comparing results from some 10 different indirect methods. These 10 methods were not measuring the same body constituent (e.g. water, intracellular water, potassium, average body specific gravity etc); the constituents were subject to different conflicting influences and different factors were being used to estimate body composition from the prime data. Added to this, several of the original studies used by Forbes were reported as falling in the <800 kcal/d category but were actually studies based on food or formula diets with protein or carbohydrate levels per day which are not considered as a VLCD according to current standards.

From the total data set it was possible to identify a total of 32 studies which used the same body composition method (variations of the hydrodensitometry method). Of these eleven studies were in the range below 600 kcal, six in the range 600-800 kcal and fifteen studies in the 800-1200 kcal categories.

Data relating to all the relevant body composition studies are described by Marks and Schrijver, 2001. The data for those studies which used the hydrodensitometry technique are shown in Figure 7.2. It shows that between 20 and 60 kg mean fat weight, there is no change in the ratio FFM/weight loss at any diet level.

Figure 7.2. A composite plot of the ratio Δ FFM/Δ weight loss against the mean fat weight. The plots represent means of at least 5 subjects using hydrodensitometry.



[Data derived from Marks and Schrijver, 2001]

Moreover, there are two extensive studies (Hoie, et al., 1993; Donnelly, et al., 1994) which provide information relating to the question of whether the proportional loss of fat free mass is greater at a lower BMI level. In the study of Hoie et al., (1993) body composition analysis was undertaken by near-infra-red interactance (Futrex 5000). It was conducted on 82 women and 45 men and a 430 kcal diet containing 61.5 g high quality protein and 30.5 g carbohydrate was consumed daily for eight consecutive weeks. The proportion of the total group in the various BMI categories at the start of dieting and after 8 weeks as calculated from these data is shown in Table 7.5. As a result of an average loss of some 3.9 BMI units for women and 4.8 units for men 20 % of the group came into the normal weight category (BMI 20-25 kg/m^2) at the end of the 8 weeks diet with a further 30 % having a BMI between 25 and 30 kg/m^2.

Table 7.5. Number (%) of dieters in each BMI range at start and end of an 8 weeks' diet

BMI Range	Number of dieters (%) week 0	Number of dieters (%) 8 weeks
20.0-24.9	0 (0%)	25 (20%)
25.0-27.9	7 (6%)	19 (15%)
28.0-29.9	19 (15%)	19 (15%)
≥30	101 (79%)	64 (50%)

[Hoie et al., 1993]

The ratio of FFM/weight loss overall was 0.25 with no significant difference between men and women. A scatter diagram of this ratio compared with the initial BMI did not differ significantly over the whole pre-diet range from 51 down to 25 ($r = -0.03$; $P = 0.75$).

The study by Donnelly et al., (1994) was conducted only in women (116) using a diet providing 520 kcal (protein 50 g, carbohydrate 79 g) for 12 weeks and with body composition determined by hydrodensitometry. Adapted from Donnelly et al. (1994), Table 7.6. indicates the number and percentage of subjects who fell into different BMI categories before and after the diet. Before dieting the lowest BMI was 27, the highest 64 (mean 37.6) and with a mean fall of 20.2 kg over the 12 weeks, the mean BMI level at the end of dieting was 30.2 with 16 subjects (14 %) achieving a normal weight (BMI<25 kg/m^2) (range 21.9 – 24.9).

Table 7.6. Number (%) of dieters in each BMI range at start and end of a 12 weeks' diet

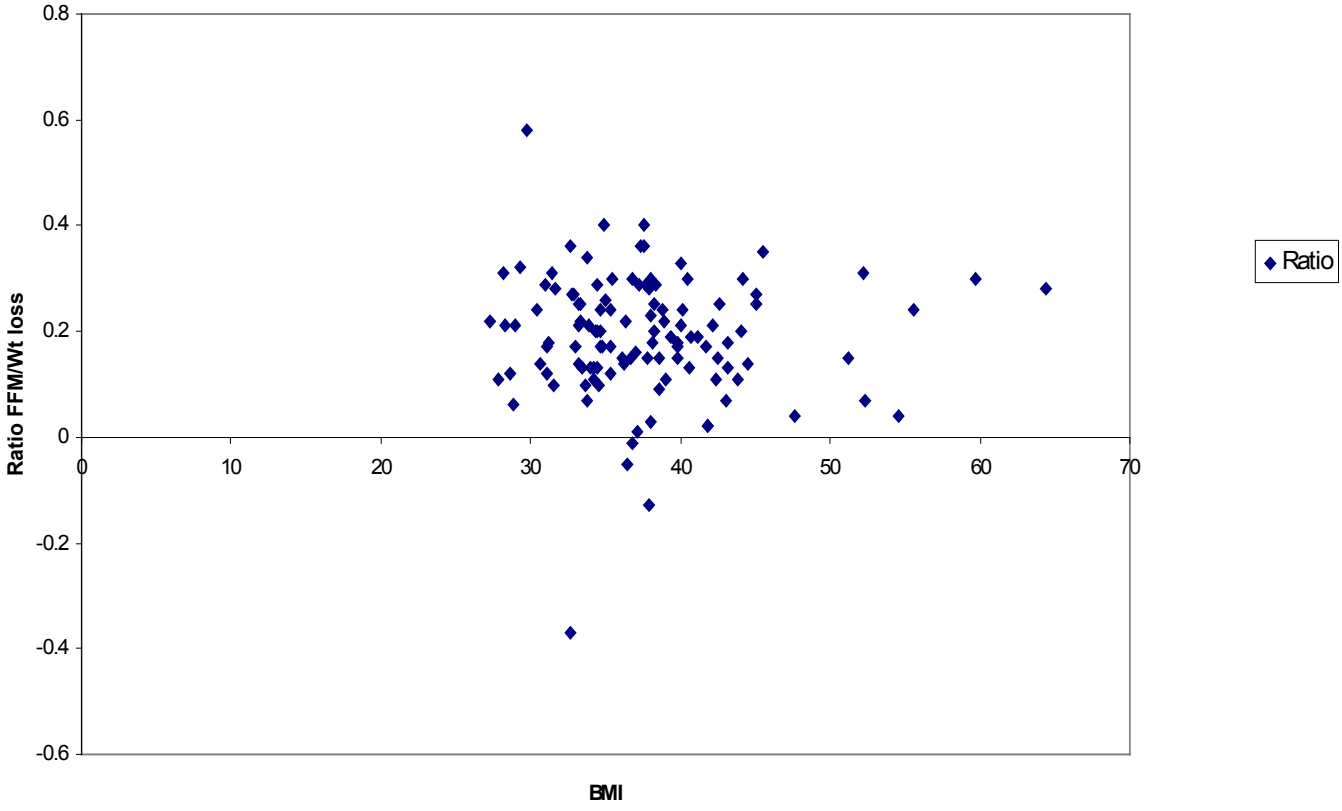
BMI (kg/m^2)	Number of dieters (%) week 0	Number of dieters (%) 12 weeks
20.0-24.9	0 (0%)	16 (14%)
25.0-29.9	9 (8%)	48 (41%)
30.0-34.9	37 (32%)	37 (32%)
35.0-39.9	39 (34%)	8 (7%)
40.0-44.9	20 (17%)	4 (3%)
≥45.0	11 (9%)	3 (3%)

[based on Donnelly et al., 1994 and additional data from Donnelly]

Figure 7.3. shows the relationship between the ratio of the FFM/Wt loss and the BMI level. The mean FFM/weight loss ratio was 0.19 confirming that there is no difference in the FFM proportional loss at different BMI levels. It is noteworthy that the level of compliance to the diet was excellent with only four dieters showing a weight loss of less than 1 kg per

week. Each of these four with poor compliance recorded a FFM/weight loss ratio that was substantially out of line including both those at the extremes of the scatter graph.

Figure 7.3. A scatter diagram of the Δ FFM/Δ weight loss ratio compared with initial BMI in 116 women dieting for 12 weeks on a 520 kcal VLCD



[Based on Donnelly et al., 1994 and additional data from Donnelly]

Although the Hoie et al. (1993) study used near infra-red interactance to measure the body composition, while Donnelly et al. (1994) used densitometry, the proportion of fat lost to weight lost was of the same order in both studies. Moreover the study by Hoie et al. (1993) was based on a relatively high daily protein ketogenic diet while that of Donnelly et al. (1994) involved a non-ketogenic diet with more modest protein content.

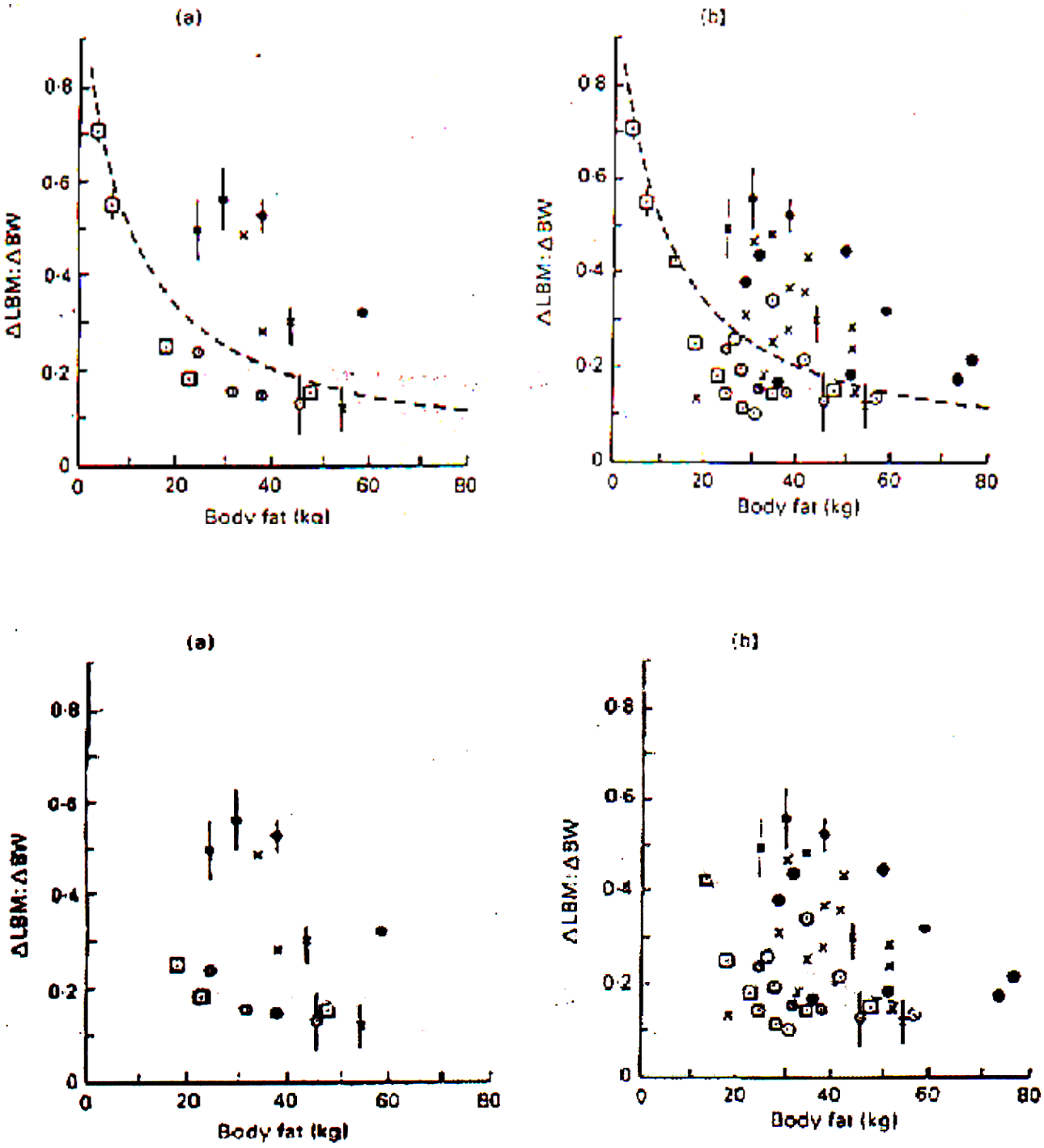
From the information derived from the 32 studies involving a relatively limited number of dieters (using VLCD and LCD) coupled with that from the two extensive studies which examined ketogenic/non-ketogenic VLCD and the two genders, it can be concluded that there is no difference in the proportion of fat which is lost during dieting:

- between LCD and VLCD;
- between men and women;
- between ketogenic and non-ketogenic diets;
- throughout the whole range of initial BMI levels from about 60 down to 25 kg/m^2;
- end of diet BMI levels in the normal range (20–25 kg/m^2).

Moreover, re-examination of the Forbes (1987) and Prentice et al. (1991) graphs demonstrates that if the two extreme data points (body fatness < 20 kg; substantially below normal levels) are excluded (Figure 7.4.), the trend as reported by Forbes disappears.

It has been held also, that the classical work of Keys et al. (1950) in the Minnesota study supports the Forbes contention. Re-examination of these data shows that this conclusion is not valid (Marks and Schrijver, 2001).

Figure 7.4. The classical Forbes (1987) (a, above) and Prentice et al. (1991) graphs (b, above); with the two extreme data points (body fatness < 20 kg) excluded (a and b, below)



7.4. Other aspects that affect safety

7.4.a. Composition of the VLCD

The compositional standards of the VLCD from which these data have been determined are given in Table 7.1. Chapter 8 considers composition and quality standards. The safety considerations reviewed in Chapter 7 are based upon the use of VLCDs of the composition defined by the working group as given in Chapter 8.

7.4.b. Precautions as to use

Chapter 9 considers the absolute contraindications to the use of VLCD, the medical conditions for which professional experience is necessary for their safe use and the general precautions which should be applied for all dieters.

7.4.c. VLCD use among children and adolescents

Increasing prevalence of obesity in children and adolescents all over the world demands primary and secondary prevention of overweight and obesity in this age group. Primary prevention focuses on establishment of a healthy, active lifestyle and keeping children and adolescents within a range of body weight which is considered to be healthy. For those children and adolescents who are already obese, secondary prevention is mandatory. Therapeutic intervention programmes for the obese aim at long-term weight maintenance and normalization of body weight and body fat. They have to modify eating and exercise behaviour of the obese child and establish new, healthier behaviour and lifestyle. In grossly obese children and adolescents under strict medical control the use of VLCDs and/or protein-sparing modified fast is possible. It must be stressed that under certain conditions VLCDs provide a safe and efficient treatment of obesity but emphasis has to be put on continuous weight control and behavioural training as well as follow-up care. In general, the opinion is that VLCD treatment in children and adolescents can be useful in superobese patients, who tried several times to lose weight with conventional diets and failed, as well as in patients with Prader-Willi syndrome.

Regarding regulation on the use of VLCDs in adolescents and younger age groups, the strong advice is given to define a contra-indication for children under 10-12 yeas of age.

Furthermore, VLCDs should never be given to adolescents without medical supervision and should never be used as a single treatment.

CHAPTER 8

Composition and quality factors

As described in Section 1.3., the members of the SCOOP working group decided at their first meeting to accept the Codex standard regulation as a working document and to discuss the issues along the given regulation, taking the scientific literature into consideration. This chapter provides also additional information about the discussion within the Codex Committee on Nutrition and Food for Special Dietary Uses (CCNFSDU).

8.1. Protein

In the Codex standard the minimal level for protein was defined as: A formula food for very low energy diet shall provide "*not less than 50 g protein with a nutritional quality equivalent to a protein-digestibility-corrected amino acid score of 1"*. It follows that minimum levels of suitable protein must be set for VLCDs in order to minimize nitrogen deficits. This depends partly upon the quantity of protein included in the diet, but also upon total energy intake. Some Codex delegations were in favour of an intake of not less than 1 g of high biological value protein per kg ideal body weight per day or even much higher, 1.2 to 1.5 g (National Task Force, 1993; Wadden et al., 1990b). For such demands the energy level of the VLCD must be at least 600 kilocalories per day. The higher amounts of proteins are required to maximize the preservation of lean body mass on very low energy diets (Froidevaux et al., 1993). The analysis on the ratio level FM/FMM loss as described in Section 7.3. do not support this view for VLCDs in the range of 400-800 kcal. As a basis of their reviews the members of the SCOOP working group accepted the minimal level of protein to be 50 g having a recognized high nutritional quality.

8.2. Fats

In order to ensure at least the minimum intake of protein and carbohydrates, the fat content of the products must, except for essential fatty acids, be kept low. Therefore, the Codex standard stated that *"very low energy diets shall provide not less than 3 g of linoleic acid and less than 0.5 g α-linolenic acid in the recommended daily intake with the linoleic acid/α-linolenic acid ratio between 5 and 15".*

The need of α-linolenic acid is not high, because there are adipose essential fatty acid reserves. Nevertheless, there is a loss of α-linolenic acid from adipose triglyceride during very low calorie dieting despite supplementation. The health significance of this reduction in adipose 18:3ω3 with rapid weight loss remains to be determined (Tang et al., 1993).

Therefore, the content of these essential fatty acids in VLCDs was based on the above Codex recommendation. VLCD containing at least 7 g of a normal fat per day reduce the incidence of cholelithiasis to that found with any diet manipulation in those with excess weight. This quantity of normal fat provides the established daily requirements for linoleic and α-linolenic acid (3.0 g and 0.5 g/d).

8.3. Carbohydrates

There was an extensive discussion on the level of carbohydrates to be set for such foods in the Codex standard. It was proposed to reduce it to 40 g. However, the Committee on Nutrition and Foods for Special Dietary Uses had finally agreed to retain the level of 50 g and to refer to 'available' carbohydrates. There has been a long-standing controversy about whether diets high or low in carbohydrate are superior in sparing protein in obese individuals undergoing hypocaloric dieting. The proposed minimum carbohydrate levels ranged from 30 g up to 100 g per day in VLCDs providing from 450 kilocalories to 800 kilocalories per day (CX/NFSDU 95/3, -Add.1, -Add. 2). Some scientists have favoured the ketogenic (low-carbohydrate) diets on the basis that ketone bodies spare protein during caloric deprivation (see Section 6.1.). Others have found little or no difference between ketogenic and non-ketogenic diets. Yet, other scientists favour the non-ketogenic diets since they have observed that isocaloric replacement of fat by carbohydrate is associated with an improved N-balance. Optimum inhibition of endogenous protein degradation and ketogenesis is only attained at a daily carbohydrate intake of 100 g per day. Endogenous gluconeogenesis in fasting individuals ranges between 2 and 2.9 g per kg body weight and day. Hence, a compensation of endogenous gluconeogenesis from amino acids and thus a conservation of endogenous protein stores cannot be achieved through minor quantities of alimentary glucose (Elia, 1991; Vazquez and Adibi, 1992). On the other hand a negative energy balance will lead to a certain endogenous protein degradation taken the composition of the body weight into consideration (ratio of 75/25 FM/FMM). Therefore both the direct protein sparing effect of addition of carbohydrate as well as the non-ketogenic property of higher levels of carbohydrate should be taken into consideration. The review by the working group was based on the level of 55 g of 'available' carbohydrates.

8.4. Dietary fiber

The question of the provision of 'dietary fiber' has not been considered in the above Codex standard. It should be stated that the dietary fiber content of products mentioned in Article 1 (2) of the Commission Directive 96/8/EC shall not be less than 10 g of a defined fiber. So far the existing literature about the beneficial effects of fiber in VLCDs are lacking as it is for most micro nutrients. The recommendation of 10 g of a defined fiber is based

rather on the general knowledge of the beneficial influence of fibers on intestinal function and on some aspects of lipid and carbohydrate metabolism. Furthermore it is generally accepted that addition of fibers in addition to the VLCD diet diminish the frequency of reported gastro-intestinal distress such as obstipation. Data are lacking to set a maximum level in the daily ration. It is suggested that levels over 30 g will cause gastro-intestinal problems. It is the opinion of the SCOOP working group that fibers should be an ingredient of a VLCD product.

8.5. Vitamins and minerals

At the first meeting of the SCOOP members it was accepted for their consideration that the proposed content of vitamins and minerals in formula foods for use in VLCDs would be based on the Commission Directive 96/8/EC of 26 February 1996 on foods intended for use in energy-restricted diets for weight reduction including minimum levels for certain vitamins and minerals (Table 8.1.).

The Codex values are derived from current FAO/WHO Recommended Dietary Intakes (for the adult male) and from the Helsinki Paper (Report of a Joint FAO/WHO Expert Consultation on Recommended Allowances of Nutrients for Food Labelling Purposes, 1990) which should be reviewed when new figures (from the FAO/WHO Expert Consultation on Human Vitamin and Mineral Requirements in Bangkok, Thailand, September 21-30, 1998) have been published. Meanwhile, a preliminary report on Recommended Nutrient Intakes (RNI´s FAO/WHO 1998) of the Bangkok consultation is available for comparison (see Table 8.1.)

It should be noted, that these new figures do not include RNIs for manganese, chromium and molybdenum. The essentiality of manganese for animals is established beyond question. In contrast, evidence of manganese deficiency in man is poor. Average basal or normative requirements for manganese cannot be established because the data required for this purpose are not available. The threshold toxicity level is also unknown. The Scientific Committee for Food of the EU estimated 1-10 mg/day as acceptable range of intake (SCF, 1993; WHO, 1996). Thus, the minimum population intake is likely to meet normative needs for manganese. The working group accepted 1 mg/d for its considerations.

Table 8.1: List of vitamins and minerals of very low calorie products (CODEX STAN 203-1995) in comparison with those for energy-restricted diets for weight reduction (Commission Directive 96/8/EC), the Recommended Nutrient Intakes (RNIs FAO/WHO 1998) and the minimum values (2000 kcal/d) in nutritionally complete medical foods (Commission Directive 1999/21/EC), respectively

	CODEX STAN 203-1995	**Commission Directive 96/8/EC**	**RNI's FAO/WHO 1998**	**Commission Directive 1999/21/EC**
Vitamins				
Vitamin A (µg)	600	700	600	700 RE
Vitamin D (µg)	2.5	5	5	10
Vitamin E (mg)	10	10	10	10 alpha TE
Vitamin C (mg)	30	45	45	45
Thiamin (mg)	0.8	1.1	1.2	1.2
Riboflavin (mg)	1.2	1.6	1.3	1.6
Niacin (mg)	11	18	16	18
Vitamin B_6 (mg)	2	1.5	1.3	1.6
Vitamin B_{12} (µg)	1	1.4	2.4	1.4
Vitamin K (µg)				70
Folic acid (µg) (as monoglutamate)	200	200	400	200
Biotin (µg)		15	30	15
Pantothenic acid (mg)		3	5	3
Minerals				
Calcium (mg)	500	700	1000	700
Phosphorus (mg)	500	550		600
Iron (mg)	16	16	14 *	10
Iodine (µg)	140	130	130	130
Magnesium (mg)	350	150	260	150
Copper (mg)	1.5	1.1		1.2
Zinc (mg)	6	9.5	7.0 **	10
Potassium (g)	1.6	3.1		1.6
Sodium (g)	1	0.575		0.6
Selenium (µg)		55	34	50
Cr (µg)				25
Mo (µg)				70
F (mg)				<4
Cl (g)				0.6
Manganese (mg)		1		1

* 10% bioavailability
** moderate bioavailability
RE stands for retinol equivalent

TE stands for tocopherol equivalent

The Scientific Committee on Food was unable to specify any requirements for chromium and molybdenum (SCF, 1993). There are only safe ranges of population mean intakes of these trace elements. Thus, the minimum population intake likely to meet normative needs for chromium might be approximately 33 µg/day. Estimates of the daily intake of molybdenum differ widely (80 - 250 µg/day). Extrapolation from animal data suggests

that the adult human basal requirement for molybdenum could be approximately 25 µg of this element per dayBased on the WHO review the estimated average requirement for this element is approximately 0.4 µg molybdenum/kg of body weight (WHO, 1996).

New magnesium balance data were used as the basis for establishing Estimated Average Requirements (EARs) for men and women aged 19 through 30 years of 330 and 225 mg/day, respectively. This results in a RDA for magnesium in men of 400 mg, and for women of 310 mg/day (FNB/IOM, 1997). The working group based their consideration on the Codex value of 350 mg (Table 8.1.).

It should be noted, that the daily quantities of micronutrients considered appropriate for healthy people on a normal mixed diet are necessarily appropriate for obese people consuming hypocaloric diets. However, severe food energy restrictions could increase the need for some and decrease the requirements for other.

The last column of the table shows the minimum values (2000 kcal/d) for vitamins and minerals in nutritionally complete medical foods which are intended to meet the particular nutritional requirements of persons affected by specific disease, disorder or medical conditions; whereas for this reason they must be used under medical supervision which may be applied with the assistance of other competent health professionals (Commission Directive 1999/21/EC). Exclusive of iron, these values are comparable with those in the Commission Directive 96/8/EC.

8.6. Ingredients

In the above Codex standard it was also established that *"Very low energy diets shall be prepared from protein constituents of animal and/or plant which have been proved for human consumption and from other suitable ingredients necessary to achieve the essential composition of the product as set out in Sections 3.1. and 3.2. above".* That means that other essential nutrients (e.g. selenium or vitamin K) not specified in the Codex Standard may also be included. The working group presumed that the nutritional substances used in the manufacture of VLCD are based on those listed in the Annex of the Commission Directive 2001/15/EC on substances that may be added for specific nutritional purposes in foods for particular uses.

CHAPTER 9

Advice on the information that should be conveyed to the consumers of VLCDs

9.1. Name of the food

Current labelling rules laid down in Directives 2000/13/EC and 89/398/EC require the names used for foods to be sufficiently precise to inform the consumer about the true nature of the food, and to enable the food to be distinguished from products with which they might be confused. In addition to the name under which a VLCD product is sold it must, like other dietetic foods, provide information about its particular nutritional characteristics.

The use of specific descriptions for VLCDs is required in some countries, the notable exceptions being Ireland, France, Sweden and the UK. The description most commonly used is "Slimming product with very low energy content intended for treatment of obesity". To ensure that consumers understand the nature of VLCDs, the labelling of these products needs to provide information about their very low energy content, and ensure they are easily distinguishable from other slimming products such as meal replacements and total diet replacements intended to be used within a regimen providing 800-1200 kcals/day.

The working group considered that VLCDs could be described as: "Slimming product with very low energy content for the dietary management of excess weight".

9.2. Nutrition labelling

VLCDs are currently required to carry, as a minimum, information about the energy value and the carbohydrate, protein and fat content of the product, as marketed, per 100 g or 100 ml as appropriate. Information per specified quantity of the product as prepared for consumption may also be given voluntarily. Additional nutrition information may be given voluntarily, in accordance with the requirements of the nutrition labelling Directive 90/496/EC, and to provide information about the suitability of the product for its particular nutritional use.

Full nutrition labelling, namely the information listed above plus the amounts of sugars, saturates, fiber and sodium is given by some but not all products. A minority of products additionally provide information about the amounts of mono-unsaturated and poly-unsaturated fats and cholesterol. All products additionally provide information about the quantities of vitamins and minerals per 100 g and/or 100 ml and the relevant percentage of the Recommended Daily Allowance.

Information about the macro- and micronutrient content of products per 100 g or 100 ml (as sold) is useful to compare different products, and for consumers the additional information about the amount of nutrients provided per serving and per day can be useful. The vitamin and mineral content of VLCDs expressed as a percentage of the relevant recommended daily allowances (RDA), is particularly important as a means of informing consumers about the adequacy of the product to meet daily requirements and its suitability to be used as a sole source of nutrition.

9.3. Contra-indications

Inventory of products on the European market has shown that manufacturers provide information on a wide range of contra-indications (absolute and relative) either on-pack, or in associated product literature. Detailed guidance for use by physicians and health professionals responsible for administering and monitoring consumers of VLCDs is also provided by some manufacturers.

These contra-indications can broadly be divided into 3 categories, namely:

- categories of persons for whom VLCDs are unsuitable;
- diseases or conditions where use of VLCDs is either absolutely contra-indicated, or where additional supervision and/or changes to treatment regimens may be required;
- other information, or conditions which should be observed for the effective and safe use of VLCDs.

9.3.a. Categories of persons for whom VLCDs are unsuitable

The suitability of VLCDs for use by specific population groups was not addressed by the SCF, in its 1990 report on foods intended for weight control diets. However, a broad consensus is reflected in the recommendations and views of expert groups across Member States. The groups for whom VLCDs are considered unsuitable as a sole source of nutrition are infants and children (under 10-12 years of age), adolescents, pregnant and lactating women, and elderly.

There is however some difference in opinion among countries about whether the use of VLCDs should be absolutely contra-indicated for certain of these groups. Although in most countries they are absolutely contra-indicated, no labelling provisions apply in The

Netherlands and Ireland. In the UK, while VLCDs are generally considered unsuitable for these groups, their use on the recommendation of a physician is not precluded.

The information given on the labels and in supporting literature for products on the EU market varies widely. Products which may only be obtained on referral from a physician (e.g., Lipotrim and Success/Lifeline diet) carry no advice. For products sold at retail the recommendations are not consistent, while all the groups listed above plus those 'doing hard physical work' are advised not to use Nutrilett, the use of Modifast is not contra-indicated for any population group.

In all countries except one, VLCDs are available at the retail level without prescription. In the opinion of the working group, in the interests of consumer protection it would be appropriate that all products sold at retail which could be used without medical supervision, should carry an appropriate and clear warning statement on the pack and in the accompanying product literature. A suggested indication might be *"the product is unsuitable as a sole source of nutrition for infants and children, adolescents, pregnant or lactating women and the elderly".*

9.3.b. Contra-indicated medical conditions

The diseases and medical conditions for which VLCDs should be contra-indicated have been widely reviewed both by European and international groups. There is broad consensus about both absolute and relative contra-indications, and these are outlined in Table 9.1.

Table 9.1. Contra-indications

Porphyria
Liver or kidney disease
Type 1 diabetes mellitus
Haemopathy
Cancer
Electrolyte disorders
Orthostatic hypotension
Cardiovascular or cerebrovascular disease, including cerebral arteriopathy
Hereditary metabolic diseases, e.g. phenylketonuria
Abnormal psychological states of more than a minor degree including schizophrenia
Behavioural disorders involving eating (bulimia or anorexia), alcoholism or drug addiction
Major surgery or serious accident within the last 3 months
Gout
Gallstones
Renal lithiasis
Acute ischaemic cardiopathies

The American Association of Clinical Endocrinologists (AACE) has published the following list of contra-indications for VLCD use. This is broadly consistent but slightly more comprehensive than the requirements and recommendations made for European products.

Contra indications to VLCDs (AACE/ACE Obesity Task Force, 1998)

- Recent myocardial infarction
- Cardiac conduction disorder
- History of cerebrovascular, renal, or hepatic disease
- Type 1 diabetes mellitus
- Major psychiatric disorders
- Gallbladder disease
- Alcoholism
- Cancer
- Infection
- Acute substance abuse
- Anorexia/bulimia
- BMI $\leq$ 30 kg/m^2

It is the opinion of the working group that contra-indications should be clearly stated on the package and in the accompanying product literature. A suggested advisory wording

could be *"the product should not be used by patients with acute or chronic diseases without consulting a general practitioner. These diseases include: cardiovascular or cerebrovascular disease, type 1 diabetes mellitus, liver, kidney and gallbladder diseases, cancer, psychiatric disorders, including eating disorders (anorexia/bulimia), substance abuse, porphyria and hereditary metabolic diseases, acute and chronic infections, electrolyte disturbances and recent surgery or serious accidents".*

9.3.c. Management of medication during very low calorie diets

Mustajoki and Pekkarinen (2001) draw attention to the fact that in their experience more than 70% of their patients in VLCD programmes are on regular medication for chronic diseases. They provide a useful table for the management of the medication during the use of VLCD (Table 9.2.).**Table 9.2. Management of other medication during the use of VLCD**

Medication	Action
Type 2 diabetes mellitus treatment with insulin or oral hypoglycaemic agents	Reduce or stop, then control (normally at lower dose) under laboratory control
Hypertension	Stop diuretics initially, reduce dose of other anti-hypertensives on basis of blood pressure values
Oral anti-coagulants (e.g. warfarin)	Continue pre-diet dose but monitor INR at frequent intervals and modify dose accordingly
Lipid lowering drugs	Stop or decrease except in familial hypercholestero-laemia
Drugs for angina pectoris, asthma, epilepsy, depression and anxiety	Continue with pre-treatment doses

[based on Mustajoki and Pekkarinen, 2001]

9.3.d. Other information or conditions for safe and effective use of VLCDs

It is the opinion of the working group that at the moment hardly any information is available about the consumer profile of individuals who use VLCDs; such as sex, age, BMI, how long etc. More consumer targeted information on the safe and effective use of VLCDs is needed.

VLCDs must be labelled with instructions for their appropriate preparation and use. All foods are required, by Directive 2000/13, to provide instructions for their preparation if it would be difficult to make appropriate use of the food in the absence of such instructions. In addition to these instructions the following key information is also usually provided by manufacturers:

- Consume adequate amounts of water (at least 1.5 l or 2 l per day depending upon the product);
- Consume the whole of the daily dose if the product is used as the sole source of food;
- If receiving medical treatment or having a medical history consult a physician before starting a diet.

Products in France and The Netherlands also carry a warning that very low calorie diets may present a health risk if they are not undertaken with the advice or supervision of a physician. The instructions for the maximum recommended duration for use of VLCDs, and advice about repeated use vary between countries. A period of no more than 3-4 weeks is generally recommended where VLCDs are used without medical supervision, although Sweden recommends a maximum of to 1-2 weeks' unsupervised use.

It is the opinion of the working group that, the following additional information could be provided to consumers on the package and in the accompanying product literature: *"the product should not be used without medical supervision for longer than 3 weeks; ample water intake of at least 2 l per day; the whole daily portion should be taken".*

Advice to consumers that VLCDs can only be used for the treatment of obesity is required for products sold in Norway, Denmark, Finland and Belgium. While it is accepted that VLCDs should ideally be used when conventional weight loss regimens have proved unsuccessful, this is not generally reflected in the labelling of products.

As VLCDs, like other foods, are required by general labelling rules to bear a list of ingredients; the appropriate durability indication; any special storage conditions or conditions of use; and the name and address of the producer/importer, it is not necessary to address these issues in this report.

9.4. Claims – rate and amount of weight loss

Many, but not all, countries have in place legislative controls or voluntary agreements which preclude manufacturers from making claims in the advertising, or labelling of VLCDs about the amount, or rate of weight loss which can be achieved by their use. In addition, claims that VLCDs can reduce feelings of hunger or increase feelings of satiety are not permitted in some countries. These requirements reflect the provisions which already

apply to total diet and meal replacements for weight control, laid down in Directive 96/8/EC on foods intended for use in energy-restricted diets for weight reduction.

The use of claims for VLCDs is controlled by Article 2 of Directive 2000/13 which broadly requires that the labelling and methods used in labelling must not be such as to mislead the purchaser to a material degree. Article 6 of Directive 89/398/EC also prohibits any dietetic food from making medical claims in its labelling, presentation and advertising.

It is the opinion of the working group that it is advisable that there should not be any indication of the amount and/or rate of weight loss achieved by the use of VLCDs.

9.5. Conclusions

In the interests of consumer choice and to ensure the safe and effective use of VLCDs certain key information should be made available to consumers. This includes the suitability of the product for the individual consumer, including contra-indications; the qualities which make it suitable for its intended purpose; and information about its appropriate preparation and use.

The following proposals reflect the information, which the working group considered to be advisable for the consumer:

- Nutrition labelling, per 100 g or 100 ml and specified quantity of the product ready for use and per daily amount, as proposed for consumption including the available energy (in kJ and kcal) and the amounts of protein, carbohydrate, sugars, fat, saturates, fiber and sodium in the product.
- The average amounts of the vitamins and minerals per 100 g or 100 ml and specified quantity ready for use, and per daily amount as proposed for consumption. This information should be expressed in numerical form, and as a percentage of the recommended daily amount.
- Instructions for the use and, where appropriate, the preparation of the product.

- A statement on the package and in the accompanying product literature that:
  * VLCDs should not be used without medical supervision for longer than 3 weeks;
  * ample water intake of at least 1,5 l to 2 l per day should be consumed;
  * the whole daily portion should be taken.
- A statement on the package and in the accompanying product literature warning consumers that VLCDs are unsuitable:
  * as a sole source of nutrition for infants and children, adolescents, pregnant or lactating women and the elderly;
  * for patients with acute or chronic diseases without consulting a physician. These diseases include: cardiovascular or cerebrovascular disease, type 1 diabetes

mellitus, liver, kidney and gallbladder diseases, cancer, psychiatric disorders, including eating disorders (anorexia/bulimia), substance abuse, porphyria and hereditary metabolic diseases, acute and chronic infections, electrolyte disturbances and recent surgery or serious accident.

The working group noticed the lack of information about the profile of the consumer of VLCDs. It recommends further research on this topic in order to be more specific in the required information to the user.

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APPENDIX 1

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