Home Artificial Nutrition: Costs and Consequences

A systematic literature review

Dissertação de Mestrado em Gestão e Economia da Saúde, apresentada à Faculdade de Economia da Universidade de Coimbra para obtenção do grau de Mestre

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Abstract

Background: Malnutrition affects health clinical status and health outcomes, occurring both in hospital and community setting. Despite recognized as a health care concern, it still is not adequately diagnosed and treated. Home Artificial Nutrition had its turning point with changes in hospital healthcare reimbursement system and development of home care technologies. Objectives: This thesis aims a better understanding of the health economics related to this home nutritional therapy, assessing the current evidence, namely on costs and consequences. Material and Methods: A systematic review of literature was made using several databases and different keyword combinations related to the subject. Complementary search was made in general search engines and other websites related with Enteral and Parenteral Nutrition. The following steps were removal of article duplication, Title and Abstract evaluation and the final selected ones were subject to full reading. Starting with an initial pool of 583 articles, 116 we were mentioned in this work. Results: Home Artificial Nutrition programs are increasingly at use around the world. Outcomes rely heavily on the underlying disease and patient Quality of Life is difficult to assess due to the differences of home nutrition programs and lack of specific tools able to measure and follow-up changes over treatment. Costs vary significantly according to countries and nutritional therapy and most of the times calculated from a payer perspective. Few studies relate costs and consequences simultaneously and most are developed from a National Health Service or Insurance perspective with a limited evaluation of a wider societal benefit. The existence of a multidisciplinary nutrition support team is crucial for the successful implementation of this therapy. Conclusions: Home Artificial Nutrition is a valid clinical alternative for clinically stable patients, allowing relocation from hospital to home with cost reduction to health care services and increase of patient Quality of Life. Harmonization should be performed in several areas: clinical and follow-up practices, accessibility, legislation and reimbursement and more scientific research is necessary for a better understanding of costs and benefits of home nutritional support. Portugal should take steps in legislative path for developing and harmonize program implementation across the country.
Keywords - Home Artificial Nutrition, Economic studies, Costs, Benefits and Reimbursement.
Resumo

Enquadramento: A desnutrição afecta o estado clínico e os resultados em saúde da população, tanto a nível hospitalar como na comunidade. Apesar de ser reconhecido como factor com impacto na saúde, ainda não se encontra suficientemente diagnosticado nem tratado. A Nutrição Artificial ao Domicílio teve maior desenvolvimento com as alterações nos sistemas de reembolso hospitalar e com o progresso das tecnologias de suporte ao domicílio. Objectivos: Esta tese visa aprofundar o conhecimento clínico e económico associado a esta terapia, avaliando os dados disponíveis, nomeadamente sobre os seus custos e consequências. Material e Métodos: A revisão bibliográfica foi efectuada em diversas bases de dados e recorrendo a diferentes combinações de palavras-chave relacionadas com o tema. Foi feita uma pesquisa complementar em motores gerais de busca e sites relacionados com Nutrição Entérica ou Parentérica. Após remoção dos artigos duplicados, procedeu-se a uma avaliação dos Títulos e Resumos e os artigos selecionados sujeitos a uma leitura integral – partindo de um total de 583 artigos, 116 foram incluídos nesta tese. Resultados: Os programas de Nutrição Artificial ao Domicílio estão em uso crescente a nível global. Os resultados em saúde obtidos com esta terapia estão muito interligados com a doença subjacente e a Qualidade de Vida do paciente é difícil de determinar dada a diversidade de programas de suporte nutricional e à inexistência de instrumentos específicos que quantifiquem a Qualidade de Vida e permitam a avaliação de variações da mesma ao longo da terapia. Os custos variam significativamente de acordo com a terapia nutricional instituída e entre os vários países sendo que, na grande maioria das vezes, os estudos são feitos na perspectiva do pagador. Poucos estudos avaliam em simultâneo os custos e as consequências e são geralmente realizados na perspectiva dos Serviços Nacionais de Saúde ou seguros privados, e não de uma forma abrangente com avaliação do impacto global na sociedade. A existência de uma equipa de suporte nutricional multidisciplinar é crucial para a adequada implementação deste tipo de programas. Conclusões: A Nutrição Artificial ao Domicílio é uma alternativa clínica válida em pacientes clinicamente estáveis, permitindo a transferência do meio hospitalar para o domicílio, com redução de custos e aumento da Qualidade de Vida do paciente. É necessária a harmonização em diversas áreas da
Nutrição Artificial ao Domicílio nomeadamente, nas práticas clínicas e de seguimento, legislação e reembolso, sendo que mais pesquisa científica é fundamental para uma melhor compreensão dos custos e benefícios desta terapia. Portugal deve legislar esta terapia nutricional de forma a desenvolver e harmonizar a sua implementação em todo o território.

**Palavras-Chave:** Nutrição Artificial ao Domicílio, Estudos Económicos, Custos, Benefícios e Reembolso.
List of Abbreviations

ADA – American Dietetic Association
AIDS - Acquired Immune Deficiency Syndrome
APNEP – Associação Portuguesa de Nutrição Parentérica e Entérica (Portuguese Association of Parenteral and Enteral Nutrition)
ASPEN - American Society for Parenteral and Enteral Nutrition
AuSPEN - Australasian Society for Parenteral and Enteral Nutrition
BANS – British Artificial Nutrition Survey
BAPEN - British Association of Parenteral and Enteral Nutrition
DAM - Disease-associated malnutrition
DRM – Disease related malnutrition
EORTC - European Organization for Research and Treatment of Cancer
ESPEN – European Society for Parenteral and Enteral Nutrition
ETF – Enteral Tube Feeding
FAACT - Functional Assessment of Anorexia/Cachexia Therapy
HAN - Home Artificial Nutrition
HEN – Home Enteral Nutrition
HPN – Home Parenteral Nutrition
ICER – Incremental Cost-Effectiveness Ratio
IV – Intravenous
KPS - Karnofsky Performance Status
NADYA - Nutrición Artificial Domiciliaria y Ambulatoria (Ambulatory and Home Artificial Nutrition)
NAIT – National Alliance for Infusion Therapy
NEPAD - Nutrición Enteral Pediátrica Ambulatoria y Domiciliaria (Ambulatory and Home Pediatric Enteral Nutrition)
NICE - National Institute for Health and Care Excellence
NST – Nutrition Support Team
ONS – Oral Nutritional Supplements
PEG - Percutaneous Endoscopic Gastrostomy
PINNT - *Patients on Intravenous or Nasogastric Nutrition Therapy*

PPS - Prospective Payment System

QALY – Quality Adjusted Life Years

RSCL - *Rotterdam Symptoms Checklist*

SENPE - *Sociedad Española de Nutrición Parenteral y Enteral* (Spanish Society for Parenteral and Enteral Nutrition)

SGA - *Subjective Global Assessment*

SINPE – *Società Italiana di Nutrizione Artificiale e Metabolismo* (Italian Society for Artificial Nutrition and Metabolism)
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CHAPTER I – General Introduction

Nutrition is a basic physiological function that allows the human body to maintain their nutritional requirements, keeping the metabolic balance for daily functions and preventing illness. Some clinical conditions make regular food and drink intake no longer possible and other situations (such as oncologic diseases) require a careful maintenance of nutritional status in order to keep the function and the immune system. Artificial nutrition consists in the administration of nutrients by Enteral Nutrition, usually when a functional gastrointestinal track is available and consisting of oral supplements or tube feeding or by Parenteral Nutrition, where solutions are given directly into a vein when the gastrointestinal track is not functional or inaccessible.

The role of hospital in society is changing, being increasingly focused in acute illness and short stays, creating the need to develop other solutions and models for treating chronic or other specific diseases. Home care is a growing area due to increasing availability of home oriented technology and the possibility to reduce expenditures for health care systems. Home Artificial Nutrition is a health care therapy consisting in the administration of medical nutrition in the home setting (or long term facilities, nursing homes) with additional support services, allowing the patient to have clinical follow-up outside the hospital setting.

Economic evaluations are recognized as a crucial factor in the decision making process for health care technologies and intend to maximize population’s well-being with the available scarce resources. For this reason therapies supported either by National Health Services or private insurances, should systematically evaluate their benefits and costs, proving its “value for money”. The work purpose is to get a better understanding of health economics related to Home Artificial Nutrition, evaluating the current evidence. In order to contextualize the health economics associated with Home Artificial Nutrition, a brief description about implementation, program design and legislative framework is presented for some countries around the world. A quick overview about the clinical conditions, underlying diseases associated with home nutritional support and available epidemiological data is also performed.
Knowledge of the present status of Home Artificial Nutrition is one of first steps for better understanding of health economics related to this nutritional support, assessing the current evidence and evaluating the impact on patient outcomes and Quality of Life and costs for the health care systems. Clinical guidance harmonization, creation of registry databases for patients, more scientific research on the area and experience sharing between countries and national institutions could help in maximizing the benefits of Home Artificial Nutrition programs. A global evaluation should be made to determine the cost-effectiveness of this home nutritional support therapy with contribution of all the stakeholders involved, from governments and payers, to groups of patients and home care providers.
CHAPTER II – Search Method

The literature review was made to select articles of Home Artificial Nutrition that focused primarily on costs and benefits in order to evaluate therapy cost-effectiveness, leaving aside those dedicated mainly to clinical issues and associated complications.

The first step consisted in electronic search on seven different databases (SAGE Journals, Elsevier Science Direct, PubMed, Springer Open, Cochrane Library, BioMed Central and B-On), between the months of November and December 2014, with different word combinations: Home Artificial Nutrition, Benefit Home Nutrition, Economic Analysis and Nutrition, Home Nutrition and Economics, Cost Effective and Home nutrition, Home Nutrition and Reimbursement and Future and Home Nutrition. No filters were pre-defined in the initial search but if too many results had been obtained, filters such as Year of publication, Search in Title/Abstract, would be added accordingly. Publication language was not restricted at this stage but later in the phase of Abstract evaluation only Portuguese, Spanish, English and French articles were considered. A brief overview of the obtained results for this systematic bibliographic search is listed Annex I – Results for systematic bibliographic search. In parallel, a free web search was conducted in general search engines (like Google) in order to reach other available sources of data. From this step search, an initial pool of 569 articles was identified.

The second search step was to check article duplication and remove them, as well as a Title analysis. If the Title evaluation was not enough for assessing suitability of articles, they were kept in the pool for further assessment. From a pool of over 320 articles obtained from the criteria mentioned above, an Abstract evaluation was performed and over 190 articles were kept (including those where abstract analysis was not enough for assessing suitability of articles) for a final full reading step. Only a few selected articles for a full reading were not available. To the article selection mentioned in the above paragraphs, 14 other were added, resulting from cross bibliographic search.

Part of the publications subject to full reading were not included in this work due to content information selection and 116 articles have been mentioned in this thesis, divided throughout the structured topics, as presented in Figure 1.
In parallel, a search on some websites related with Enteral and Parenteral Nutrition was made, in order to obtain a wide picture of this clinical therapy across the world.

Figure 1 attached in the following page presents the search strategy adopted in the current work, showing the different phases followed and the output obtained after each phase was completed.
Figure 1 – Search method for literature review.

**KEYWORDS:**
- Home Artificial Nutrition
- Benefit Home Nutrition
- Economic Analysis and Nutrition
- Home Nutrition and Economics
- Cost Effective and Home nutrition
- Home Nutrition and Reimbursement
- Future and Home Nutrition

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**Keywords Analysis:**
- Malnutrition: 9 articles
- Home care: 12 articles
- Home Artificial Nutrition: 5 articles
- HPN and HEN: 29 articles
- Implementation & Legislation: 21 articles
- Economic evaluations: 10 articles
- Studies evaluated: 28 articles
- Future in HAN: 2 articles
CHAPTER III – Malnutrition

Malnutrition is defined as a nutrient imbalance affecting adversely body functions and health clinical status. It can be divided in undernutrition (lack of nutrients) or over nutrition (excess of nutrients) (Lochs, 2006) but, for the purpose of this systematic literature review, it will be regarded as undernutrition only.

Deficiency of nutrients such as protein, vitamins and minerals impacts body regular functioning and clinical outcomes, increasing patient susceptibility to disease (NICE, 2006). Undernutrition is then considered a risk factor in health outcomes (with impact on morbidity and mortality) by delaying clinical recovery and increasing the number and severity of complications associated with infections and primary diseases. It is regarded as a public health problem, that increases the use of healthcare services (more visits to family doctors, more prescriptions, increased likelihood of hospital admission with the corresponding increase of healthcare costs, among others) and is associated with a decrease in patient Quality of Life (Russell, 2007; Inotai, 2012).

Patient malnutrition is found in all healthcare settings, including home care and long care facilities and, because it often coexists with a primary disease, its impact is frequently evaluated by the number and severity of complications associated with the disease and other infections, the called Disease Associated or Related Malnutrition (DAM or DRM).

Some studies reflect the monetary impact of malnutrition in society, namely about the impact of disease related malnutrition, in several European countries and in Europe as a block.

A wide study (Inotai, 2012) intent to calculate the financial and health burden of disease related malnutrition in Europe. The model has been developed to determine the incremental health care cost and health lost (increased mortality and reduced quality of life, expressed in quality adjusted life years lost) for ten primary diseases: stroke, coronary heart disease, breast cancer, colorectal cancer, head and neck cancer, chronic obstructive pulmonary disease, dementia, depression, musculoskeletal disorders and chronic pancreatitis. Cost calculation was based on the increased number of hospital days
and hospital cost, long term nursing and drug expenditure; the utility variation (in patients with Disease Associated Malnutrition compared with those without this condition) was based on a single study and used in all ten primary disease areas. Results for 2009, show incremental financial burden over 31 billion euros, 5.7 million years of life lost (9.1 million Quality Adjusted Life Years) among the 835 million citizens of fifty European countries and Israel. The total direct health care costs and the financial value of lost Quality Adjusted Life Year were over 305 billion euros in Europe for the ten mentioned diseases.

A report from the Advisory Group on Malnutrition in the United Kingdom (BAPEN, 2008) show that the disease related malnutrition in 2007 had a public expenditure of over 13 billion pounds annually. More than three million people in the United Kingdom are either malnourished or at risk of malnutrition, 93% of them living in the community, 5% on care homes and just 2% in the hospital setting and the majority of population at risk are below 65 years. In 2006 for an invited editorial, Elia (Elia, 2006) referred that the cost of disease related malnutrition would correspond, in the United Kingdom, to approximately 10% of total expenditure on health. Another study for the United Kingdom reality (Guest, 2011) compared the clinical outcomes and healthcare resource use in two sub-groups of patients (around 1000 patients in each) in the community: malnourished and non-malnourished, for six months after the diagnosis. The cost of managing malnourished and non-malnourished patients for the National Health Service was 1753 pounds and 750 pounds, respectively, reflecting an incremental cost of over 1000 pounds, due to health care consumption increase.

In Netherlands (Freijer, 2013), additional costs of disease related malnutrition in hospital and non-hospital setting were subject to analysis, at a national level and for all health care sectors. The additional direct costs (considering prevention, diagnostics, therapy, rehabilitation and disease treatment) were estimated to be 1.9 billion euros (in 2011), corresponding to 2.1% of health care expenditure and 4.9% of total costs in hospital care, nursing and residential home, and home care setting. Of the total value, 24% (453 million euros) correspond to nursing and residential homes and 10% (185 million euros) to home care setting. According to the author, total value obtained is in line
with other European countries, and is considered conservative since is only performed in a health care perspective, on direct health care costs and excluding the pediatric population (those under 18 years old).

In Croatia, a study from the budget holder perspective has been done, to determine the economic impact of undernutrition in several chronic diseases, frequently accompanied by undernutrition (cancer, chronic pancreatitis, inflammatory bowel disease, hepatic encephalopathy, chronic obstructive pulmonary disease, chronic renal insufficiency requiring dialysis, cerebrovascular disease, pressure ulcers and femoral fractures) in population over 65 years old (Benkovic, 2014). The total cost (direct costs only) of disease-related undernutrition for selected diagnoses in adult population was over 97 million Euros, accounting for 3.4% of the total Croatian national health care budget, with the average cost, per person, of 1640 euros (referring to the year 2012). The largest share of cost was due to medication (over 40%), followed by hospitalization (over 30%) and only 6.7% of the total amount was spent on enteral and parenteral nutrition.
CHAPTER IV - Home artificial Nutrition

Home care programs are defined as a structured deliverance of equipment, service support and follow-up to the patient in the home setting, being considered a dynamic and increasing component of health care systems worldwide and appearing as a viable alternative for standard hospital care (Gorski, 1996; Corrado, 2001). In recent decades, technical development and breakthrough technologies emerged, offering multiple benefits for home health care programs (Baxter, 2005). Some clinical techniques, restrained until a few years ago to hospital environment, had become available in the home care setting like mechanical ventilation, infusion therapy, hemodialysis, peritoneal dialysis, artificial nutrition, cardiac monitoring, apnea monitoring, pain management, among others (Silver, 2002).

The expansion of home and other care sites, as viable alternative to hospital stay, had its boom in the eighty’s, namely in the United States, due to implementation of prospective payments in hospital reimbursement, reducing length of stay and resulting in earlier discharges (Gorski, 1996; Williams, 1998). Prospective Payment System (PPS) can be defined as a paying method where reimbursement is based on a pre-established value defined for a specific diagnosis, encouraging and promoting providers to deliver an efficient and outcome-based service, avoiding the resource overuse. Following this change, insurance companies increased the pressure for reducing health care costs and commercial companies providing home care service, had grown expressively, leading to a shift of healthcare spending from hospital to community (Cade, 1997). Other circumstances contribute for the increase use of home care technologies: the improved survival for chronic diseases, general population aging (Gorski, 1996) and the need to efficiently allocate scarce resources, due to financial, personal and material constrains in most healthcare systems (Baxter, 2005).

In many cases, the home care model integrates both hospital and home setting, allowing patients to undergo medical and nutritional care at the hospital or at home, assuring service standardization for quality and safety maintenance (Waitzberg, 2007). Home care schemes differ significantly according to the type of disease, patient and
complexity of treatment; nevertheless, general criteria should be taken into account when comparing home and hospital treatment, such as: obtained outcomes should be good or better, total costs should be equal or less and program implementation should be acceptable for patients and caregivers (Corrado, 2001).

Benefits of home care programs are widely recognized and present advantages for both healthcare providers and for the patient and family. From the health care provider perspective, there is a decrease of health care costs due to reduction of hospital stays and early discharges (avoiding costs associated to physical space, hospital workforce, use of equipment and technology), promoting resource optimization. From the patient point of view benefits are, among other, the diminished risk of nosocomial infections, maximization of patient comfort and dignity, independence and participation on care, increase Quality of Life and wellbeing (Gorski, 1996; ADA, 1999; Corrado, 2001; Baxter, 2005). Disease humanization is a modern concept, where a patient well-being is considered as a crucial part of the treatment, and home care is a key point in this philosophy (Moreno Villares, 2004). In contrast, home care programs also present disadvantages such as the increase burden and responsibility on informal caregivers, since they are increasingly relied to manage home care technologies (Gorski, 1996; Corrado, 2001).

Patient and family training through educational interventions is crucial (Silver, 2002) to ensure that technologies are properly handled and to deal correctly with complications that might arise during treatment. From the healthcare provider (or commercial companies responsible for providing home care) a good support system is mandatory in order to meet clinical and patient expectations, ensuring this way, quality of service and patient safety.

Home care agencies provide, nowadays, a wide range of service to patients and their families with the purpose of promoting, maintaining or restoring health and independence while, at the same time, try to reduce the effects of illness or disability (ADA, 1999). The increase of home care providers has been substantial, with an estimation of home health employees, in these companies, around 867,000 people in
2006, just for the United States, reflecting the support given to more than 7.6 million people in 2007, with annual expenditures rising over 57.6 billion dollars (ADA, 2009).

The existence of few randomized controlled studies with hospital in-patients and at home setting raises some uncertainty about the cost-effectiveness of some of these home care programs.

Home Artificial Nutrition (HAN) is a health care therapy consisting in the administration of medical nutrition in the home setting (or long care residences for older people and nursing homes) with additional support services, allowing the patient to have nutritional support therapy outside the hospital setting. Clinically, it can be defined as the administration of nutrients on the patient’s residence, with the goal of improving or keeping the adequate nutrition status, avoiding undernutrition. It can be divided in HEN (Home Enteral Nutrition) and HPN (Home Parenteral Nutrition) and this nutritional support present benefits like keeping (or increasing) patients Quality of Life, increasing social integration, avoiding risks associated with hospitalization and reducing healthcare costs (Villar Taibo, 2008).

This home nutritional support is only possible when patients do not require further stay in the hospital and have their underlying diseases and clinical situation duly stabilized that, otherwise, would have to stay in the hospital for long periods or even permanently (University of Bologna, 1995). This concept is aligned with the observed change in hospital role, being more focus on acute and critical patients (Álvarez Hernández, 2008) but also with a de-hospitalization trend allowing patient humanization and a better social integration. Other clinical features that should be followed when evaluating home nutrition support implementation is therapy restriction to those patients not able to fulfill nutritional requirements by regular food ingestion and, whenever possible, Enteral Nutrition should be preferred over Parenteral Nutrition (Moreno Villares, 2004).

A model integrating hospital and home setting, allows standardization of the nutritional services and clinical protocols, as well as harmonization in the selection criteria (Baxter, 2005). Not only patients discharged from hospitals can benefit this therapy but
also those that, due to evolution of the underlying disease, need to adopt home support measures in order to keep or improve their nutritional status (Tejada Domínguez, 2011).

Home Artificial Nutrition is part a wide concept of modern medicine that considers care in an integrated way, between hospital and home (Álvarez Hernández, 2008) and, as mentioned above for the home care programs, had a turning point in the eighties, associated with changes in hospital healthcare reimbursement, leading to the expansion of home and alternative care sites (Williams, 1998). For this reason, this home support therapy gained popularity, attracting experienced nutrition clinicians, increasing the reimbursement flexibility and developing clinical protocols for home care, leading to an increase use of Home Artificial Nutrition, when quality and patient safety are assured.

As with other home care programs, technology improvement played a crucial role in the grow of support services in the home care setting and, in the case of Home Artificial Nutrition, the development by the pharmaceutical industry of nutritional formulas, infusion pumps and other associated systems should be highlighted. Other important feature was the creation of specialized Nutrition Support Teams (NST), responsible for planning and coordinating program implementation, establishing of nutritional goals and training program, and assuring the follow-up and clinical monitoring (Planas, 2002; Tejada Domínguez, 2011).

This clinical home care support is applied in all age groups, from premature infants to the elderly (ADA, 1999). Family ability to cope with the challenges presented by home technologies must be evaluated, to ensure patient safety and the correct handling of possible complications. Patient and family caregivers must balance the advantage of being at home with the challenges of administering complex therapies and the additional support needed on a physical, emotional, social and even financial level, in order to reduce the associated burden (Winkler, 2006).

The need of Home Artificial Nutrition is, in the great majority of cases, associated with underlying diseases that, by one way or another, does not allow the patient to keep their optimal nutritional status. The most recurrent indications for HAN (both Home Parenteral Nutrition and Home Enteral Nutrition) are oncologic diseases, non-oncologic gastrointestinal diseases (like Crohn's disease, ischemic bowel disease and motility
disorder), neurological impairments and swallowing limitations. Home Artificial Nutrition is increasing on a yearly basis due to social, medical and economic factors.

**Home Parenteral Nutrition**

Parenteral Nutrition is defined as the administration of nutrients directly into a vein (central or peripheral vein, according to the clinical situation). The delivery of nutrition intravenously should only be used when it is not possible to comply with nutritional requirements through oral or enteral nutrition or when gastrointestinal track is not available or functional. This nutritional support therapy is very complex, involving the correct handling of several techniques and presenting higher risk of complications and with more serious consequences. Administration can be performed in a cyclical way (for example overnight only) if the patient can ingest liquid, or through continuous administration (Martínez, 2004).

Historically, Home Parenteral Nutrition programs had started in late sixties in the Unites States, early seventies in Denmark and in the eighties in countries like Spain and France (Moreno Villares, 2004; Aatmani, 2006). This nutritional support program might be provided by hospitals services, home infusion companies or other home health care companies (Ireton-Jones, 2003).

As occurring for other home care programs, Home Parenteral Nutrition should only be initiated after a complete assessment, demonstrating that expected benefits clearly outweigh the risks. It can be used for short term period or for life-time dependence and a smooth transition from hospital to the home setting is crucial for successful program implementation (Ireton-Jones, 2003). A strict follow-up in needed, requiring a well-organized healthcare network that can ensure a quality and safe administration, and patients have to be clinical stable and capable to be evaluated.
Epidemiology

A crucial factor for evaluating the impact of any health care program is to have an overall picture about the epidemiology of patients undergoing this therapy. For this reason a brief approach on prevalence, underlying disease, mean age and mean therapy duration for HPN is performed in the following paragraphs.

The reported prevalence of Home Parenteral Nutrition varies greatly in different countries and in different years.

In the United States, between 1989 and 1992 the average yearly prevalence of Home Parenteral Nutrition in general population was 120 patients/million inhabitants, corresponding to approximately 40,000 patients in HPN on 1992 (Howard, 1995; Williams, 1998; Moreno Villares, 2004; Álvarez Hernández, 2008). In 1992, a prevalence of 140 patients/million inhabitants has been calculated (Howard, 2000), but other authors refer lower values, such as 80 patients/million inhabitants (Pironi, 1995; Martínez, 2004). The registry responsible for data collection mentioned above stopped on the nineties, due to cost maintenance, but a new web based registry has been developed in 2011 to collect information and data about patients on Home Parenteral Nutrition (Guenter, 2012).

In European countries, prevalence values range significantly among them. Back in 1997, Home Parenteral Nutrition prevalence was estimated to be 12.7 patients/million inhabitants in Denmark, 3 to 4 patients/million inhabitants in United Kingdom, Netherlands, France and Belgium and less than 2 patients/million inhabitants in Spain and Poland (Planas, 2002; Martínez, 2004). More recent data point to prevalence rates around 24.5 patients/million inhabitants in Italy for 2005, 12.5 patients/million inhabitants in United Kingdom for 2006 (Juana-Roa, 2011), 14 patients/million inhabitants in Scotland and 9.5 patients/million inhabitants in England (Álvarez Hernández, 2008).

Some studies have been performed at national or regional level to determine the use and the characteristic of Home Parenteral Nutrition. In Italy, a study performed for the vast majority of regions, has estimated prevalence for Home Artificial Nutrition (in 2005) of 153 patients/million inhabitants and 28 patients/million inhabitants for Home Parenteral Nutrition, representing 15% of the total HAN situations (SINPE, 2007). Another
study for an Italian region (Campania) showed an increase in the number of HPN patients from 156 in April 2005 to 306 in April 2012, representing a growth of over 95% (Santarpia, 2014).

In Spain, a study based in questionnaire responses by hospitals across the country (Juana-Roa, 2011), estimated for 2008 a prevalence for Home Parenteral Nutrition of 4.9 patients/million inhabitants in Spain (5 patients/million inhabitants in adults and 4 patients/million inhabitants for children), totalizing 228 patients. An increase of the number of patients undergoing HPN was noticed, when comparing to the year 2000, where only 67 patients were on HPN throughout Spain (Martinéz, 2004). More recent data collected by Spanish group for HAN - Nutrición Artificial Domiciliaria y Ambulatoria (NADYA), reach to a prevalence of 4.0 patients/million inhabitants per year in 2011 and 4.4 patients/million inhabitants per year in 2012 (NADYA, 2014).

In Switzerland, an epidemiological study accounted new cases of Home Artificial Nutrition from 2005 to 2009 (Shaw, 2013) and from a total number of almost 13,000 new cases, only around 3% (433) corresponded to Home Parenteral Nutrition.

In another part of the world, prevalence for Home Parenteral Nutrition in 2006 for Australia and New Zealand was estimated to be 5 to 7 patients/million inhabitants (Gillanders, 2008).

For the primary diagnoses that trigger the need of HPN treatment, information was assessed for the United States (period between 1985 and 1992) and Europe (1997 data, in adults only) and the three most frequent underlying diseases for this clinical therapy were oncologic diseases, followed by Crohn’s disease and Ischemic Bowel (Howard, 2006). Other study point out that the most frequent indications for Home Parenteral Nutrition are short intestine syndrome, Crohn’s disease and active cancer (Moreno Villares, 2004) and two other authors (Williams, 1998; Howard, 2000) consider cancer as the main cause for HPN, followed by Crohn’s disease. In children, congenital gastrointestinal diseases are the leading cause (NADYA, 2014).

Data in Italy, reporting to 2012, show oncologic disease as the major condition for HPN implementation, followed by benign chronic intestinal failure (Santarpia, 2014) and in Spain, the main indications for HPN were gastrointestinal diseases (such as
mesenteric infarction, changes in motility, Crohn’s disease) followed by oncologic situations (Martinéz, 2004), confirmed by 2003 data, showing that benign intestinal diseases account for 79% and active cancer for the remaining 21% of total patients on HPN in Spain (Álvarez Hernández, 2008). Data collected in France between 1993 and 1995, show as the first cause mesenteric infarction, followed by Crohn’s disease. Despite no significant change until 1997, there was a decrease use in patients with Acquired Immune Deficiency Syndrome (AIDS), due to new therapy introduction and increase use in oncologic patients (Aatmani, 2006). In Scotland, data on Home Parenteral Nutrition in adult population collected between 2000 and 2007 (Hallum, 2012) indicate that Crohn’s disease was the main cause, responsible for 34% of total new cases.

This therapy seems to be more frequent in adults aged between 40 and 60 years old, as point out by several authors: between 51 and 64 years old (Silver, 2002) and between 40 and 60 years old (Moreno Villares, 2004; Hallum, 2012). Studies also mentioned mean patient age: 50-52 years old in adults in 2011 and 2012 in Spain (NADYA, 2014) and 47 years old in Scotland (Hallum, 2012). Mean treatment duration for an HPN patient ranges from 4.7 months (Shaw, 2013), 7.5 months (Martinéz, 2004), 8.5 months (Álvarez Hernández, 2008) to 24 months, that can go, in specific patients up to 8 years on this nutritional support (Hallum, 2012).

Despite differences in numbers, it seems clear that Home Parenteral Nutrition programs have a steady increase in the last decades and prevalence is higher in the United Stated when compared with European countries. The prevalence of Home Artificial Nutrition, including Home Parenteral Nutrition, in United States is referred as four to ten times higher when compared with other western countries (Howard, 1995), and yearly prevalence for HPN in the Unites States three to ten times higher than Europe (Howard, 2000). Some probable causes can be identified for this prevalence difference, like the extended use in cancer patients, pressure for shorter hospital stays and higher coordination between hospital centers and primary care in the United States. These factors associated with an early start of HPN program implementation lead to a much more developed commercial home care sector in the United States (Moreno Villares,
2004). Part of the difference is also explained by how prevalence is assessed in the United States that consider a yearly prevalence, and in some European countries that consider one day prevalence (Howard, 2000). This different calculation method has impact on final results since evaluation for one year time period includes new patients starting therapy and those who die or return to normal eating; while one day prevalence only includes those effectively on Home Parenteral Nutrition (Howard, 1995).

From the above, we can verify that the main two causes for this nutritional support are active cancer and gastro-intestinal diseases. The more common age of patients undergoing HPN is between 40 and 60 years old and the mean treatment duration might range from a few months up to a couple of years. Clinical evolution depends significantly on the underlying disease and patient age. Better survival is to be expected on benign gastro intestinal affections in comparison with patients with active cancer or AIDS (Moreno Villares, 2004).

**Home Enteral Nutrition**

Enteral Nutrition term includes all forms of nutritional support that uses “dietary foods for medical purposes” as mentioned in European Commission Directive 1999/21/EC of 25 March 1999. It includes Oral Nutrition Supplements (ONS) and Enteral Nutrition through a tube feeding - Enteral Tube Feeding (Lochs, 2006), and is recommended when patients are not able to meet their nutritional status orally, by standard deglutition, providing all or part of the necessary nutrients to assure regular clinical body function.

Oral Nutritional Supplements usually contains a mixture of nutrients (protein, carbohydrate, fat) and are given orally through different formulations like liquids, powders, desert like, bars. They are considered useful for several acute and chronic diseases as well as for chirurgical patients in pre or post operatory (Stratton, 2006).

Enteral Nutrition through a tube feeding is the delivery of nutrients directly into the gut, via tube and distal to oral cavity. Enteral Tube Feeding is divided according to the administration route: nasoenteral if given through the nose, gastrostomy if placed directly
into the stomach or jejunostomy if placed directly into the jejunum. Nasoenteral tubes can be divided in nasogastric (if placed into the stomach), nasoduodenal or nasojejunal if placed until the duodenum or the jejunum, respectively (Stratton, 2006; Howard, 2009). Within the gastrostomy tubes, the most frequent is the Percutaneous Endoscopic Gastrostomy (PEG) which involves a tube placed endoscopically through an incision in the abdominal wall and into the stomach and, as recommended by European Society on Enteral and Parenteral Nutrition (ESPEN), is to be preferred when the duration of enteral nutrition is expected to be longer than four weeks.

Historically, Enteral Nutrition had its roots in the early nineteen century when rubber tubing became available. At the beginning of the twenty century, nasoenteral tubes had their early development accompanied, later on, by advances in protein hydrolysate formulas and automatic feeding pumps (Vanek, 2008).

This nutrition support therapy can be applied for a few weeks or throughout an entire life and can be administered in all healthcare settings, from home care and long term care to acute care settings and in a diverse patient population.

Enteral Nutrition should be the first choice route of nutritional support, when compared to Parenteral Nutrition, due to physiological advantages (such as preventing intestinal atrophy), lower incidence of complications and morbidity, and with a lower cost (Harsányi, 1999; Klek, 2011). Food in the gastrointestinal track is very important to preserve normal physiology, increase immune function and reduce inflammation (Seres, 2013) and Home Enteral Nutrition accounts for 80% to 90% of the total of Home Artificial Nutrition, both in Europe and the United States (Pironi, 1995).

**Epidemiology**

As done for Home Parenteral Nutrition, an overall picture about the epidemiology of Home Enteral Nutrition is performed in the following paragraphs.

It is difficult to determine the prevalence of Home Enteral Nutrition in worldwide basis since, in addition to differences in registry, databases and follow-up, some countries only consider Home Enteral Nutrition when nutritional support is given through a tube
feeding, while others already consider Oral Nutritional Supplements as part of a wider concept of Home Enteral Nutrition (Moreno Villares, 2004).

Data from the United States back in 1992, estimated a prevalence of around 400 patients/million inhabitants on Home Enteral Nutrition, corresponding to 152,000 patients on this nutritional therapy (Howard, 1995; Williams, 1998; Howard, 2000; Kovacevich, 2005), value much higher when compared with other western countries. Other authors point to higher prevalence values for Home Enteral Nutrition in United States, ranging from 460 patients/million inhabitants (Moreno Villares, 2004; Villar Taibo, 2008) up to 800 patients/million inhabitants (Martinéz, 2004). A survey conducted by the National Center for Health Statistics indicate that, for the year 2000, 30,700 patients out of a total of 1,355,300 home care patients in the United States were receiving Enteral Nutrition (NAIT, 2010).

In Europe, a study performed on 1998 based on questionnaires response, had evaluate the implementation of Home Enteral Nutrition in eight countries (Belgium, Denmark, France, Germany, Italy, Poland, Spain and United Kingdom). The reported median incidence of new cases was around 163 patients/million inhabitants per year, value considered two to three times lower when compared with United States (Hebuterne, 2003).

Some European countries have collected their own data to assess implementation of Home Enteral Nutrition.

A study performed by the British Artificial Nutrition Service (BANS) has estimated that, in the United Kingdom at the end of 1998, over 12,000 patients were on Home Enteral Tube Feeding, showing an important increase, when compared to estimations of around 1,000 patients on 1990 and 6,000 patients in 1995, as mentioned by the Parenteral and Enteral Nutrition Group of the British Dietetic Association (Russell, 2001). In three English regions, the point prevalence between 1997 and 1999 was calculated to range between 150 and 280 patients/million inhabitants (BANS, 2001).

Data from a French study between 2011 and 2012 (Lescut, 2013), performed in 15 administrative regions in the country, establish an average incidence of Home Enteral Nutrition around 250 patients/million inhabitants per year and a prevalence of 573
patients/million inhabitants per year (Crenn, 2014). Projection from this number to the population of 65.5 million inhabitants in France, would lead to approximately 37,500 patients on Home Enteral Nutrition per year.

In Italy, a study evaluated the epidemiology of Home Enteral Nutrition between the years of 2001 and 2005 (Paccagnella, 2008). Mean incidence and mean prevalence were respectively 309 and 380 patients/million inhabitants per year, with growing incidence throughout the study. Another study in 16 of 20 Italian regions showed a prevalence of 128 patients/million inhabitants on Home Enteral Nutrition (SINPE, 2007).

In Germany roughly 140,000 patients were receiving Home Enteral Tube Feeding in 2000 (Loeser, 2003) and for the same year, almost 3,000 patients were on HEN throughout Spain, according to NADYA (Martinéz, 2004; Álvarez Hernández, 2008).

For the Spanish reality, prevalence is estimated to be 75 patients/million inhabitants if considering both tube feeding and oral supplements and 40 patients/million inhabitants if considering tube feeding only (Moreno Villares, 2004; Villar Taibo, 2008).

In Brazil, incidence and prevalence estimated for a specific country region, were reported to be 148 new patients/million inhabitants per year and 176 patients/million inhabitants per year, respectively (Zaban, 2009).

Major indications for Home Enteral Nutrition are neurological disorders and oncologic diseases, such as head or neck cancer (Williams, 1998; Howard, 2000; Loeser, 2003; Moreno Villares, 2004; Martinéz, 2004).

A 1998 study (Hebuterne, 2003) collecting data from eight European countries (Belgium, Denmark, France, Germany, Italy, Poland, Spain and United Kingdom) concluded that the leading underlying disease for this nutritional support was neurologic disease (49%) followed by neck and head cancer (27%). Percutaneous Endoscopic Gastrostomy (PEG) was the most used clinical technic with almost 60% of total, followed by nasogastric tube, with almost 30%.

For a specific Italian region a 5 year epidemiological study, between 2001 and 2005, followed 655 patients on HEN. Neurodegenerative disease was the main indication with 41% of total patients, followed by neurovascular disease with 27% and cancer with 21% (Paccagnella, 2008). Data from 2012 show the first cause for Home Enteral Nutrition
to be neurological disease followed by oncologic pathologies and the number of patients on HEN between 2005 and 2012 had increase significantly (Santarpia, 2014).

In Spain several studies have assess the characteristics of Home Enteral Nutrition program implementation. In Galicia region, a retrospective review made on 237 patients undergoing Home Enteral Nutrition, indicated neurologic (40%) and oncologic diseases (32%) as the most frequent underlying diseases (Villar Taibo, 2008). Another retrospective and descriptive study was performed in Zaragoza hospital between the years of 1994 and 2001 (Ocón Breton, 2002) and 101 patients on Home Enteral Nutrition were followed. The great majority of patients (almost 70%) were receiving this clinical therapy due to neurological diseases, followed by oncological diseases (17%) and digestive non-oncological diseases (9%). Another study focusing on pediatric population has been performed by the Pediatric Ambulatory and Home Enteral Nutrition (in Spanish NEPAD), where 952 patients between 2003 and 2010 were followed. Neurological and neuromuscular disease account for 30% of total cases, followed by digestive disorders (18%) and oncologic (15%). This home nutrition program has been delivered via a nasogastric tube in 55% and by gastrostomy in 36% of cases (Pedron-Giner, 2013).

A study with data from Brazil in 2005 (Zaban, 2009) showed the three more frequent pathologies that led to Home Enteral Nutrition program implementation were neurological disease (34%), followed by gastrointestinal diseases (27%) and oncological (14%). For the same year, 184 children and adolescents (under 18 years old) were followed and the main indications listed were digestive disorder (55%) and neuromuscular disease (21%) with a patient mean age of 2 years. The prevalence of HEN for children was estimated to be 81 patients/ million inhabitants in 2005 (Zaban, 2010).

Patients undergoing HEN are mostly children and elderly (Moreno Villares, 2004) and, in Europe, around 30% of total patients have less than 20 years old and more than 50% have over 60 years old (Álvarez Hernández, 2008) or, according to other reference (Hebuterne, 2003), more than half of patients were over 65 years when started Home Enteral Nutrition and 21% were over 80 years old. This is confirmed by other European national studies: in Italy the estimated mean patient age was 77 years old, with 65% of patients older than 75 years (Paccagnella, 2008); in Spain mean patient age ranges from
71 years old (Ocón Breton, 2002) to 75 years (Villar Taibo, 2008). In Brazil, for 2005, almost half of HEN patients were children (46%), followed by elders with 35% and adults have not reached to 20% of all patients (Zaban, 2009).

Mean treatment duration in HEN patients, ranges from 4 months (Villar Taibo, 2008) to 6.3 months (Martínez, 2004) in Spain, to 6.5 months in Italy (Paccagnella, 2008) and 6.5 months for Oral Nutritional Supplements and 8.5 for Home Enteral Tube Feeding in Switzerland (Shaw, 2013). A study focusing only in pediatric HEN patients in Spain, revealed a mean treatment duration of 4 months (Pedron-Giner, 2013). Despite the above mentioned numbers it is not rare that patients maintain this nutritional support for more than one year.

As with Home Parenteral Nutrition programs, Home Enteral Nutrition programs in the United States seem to be more frequent than in European countries. The available prevalence of HEN is very variable and most of the time difficult to compare due to a number of reasons: different interpretation on what is considered Home Enteral Nutrition program, different study years, different presentation of prevalence values (some consider yearly prevalence and others point prevalence), data obtained from specific country regions might not be directly extrapolated to national reality and some studies also refer to new cases verified per year – incidence. Epidemiology on most frequent indications for HEN implementation, are relatively consensual: neurological disorders and oncologic diseases are responsible for the majority of cases. Unlike HPN, the most common age groups for patients on HEN are the children and the elderly, with mean age for adults on this nutritional support above 70 years old. Mean treatment duration ranges between 4 and 9 months, but frequently patients can maintain this therapy over 12 months.
CHAPTER V – Implementation & Legislation

Numerous features contribute to a different program implementation of Home Artificial Nutrition around the globe. Legislative framework is a key point to establish the ground for nutrition support implementation in countries and should be performed taking into account the payers, service providers and, above all, patient well-being. As an example, prescription and reimbursement depend, in some countries, on the clinical condition and, in others, on the application route to be used, leading to differences in access for patients with the same clinical conditions. In this chapter we will focus our attention in HAN reality in different countries, including Portugal.

Europe

Despite being an expanding area for the last 30 years, Home Artificial Nutrition in Europe has been developed based on various national regulations and, in some cases, nutritional support programs were implemented prior to the existence of any type of regulation. A survey made in several European countries (Austria, Belgium, Croatia, Czech Republic, Denmark, France, Germany, Israel, Italy, Poland, Spain and United Kingdom) by an ESPEN Working Group, consisting in two structured questionnaires, show that most of the countries have written guidelines about implementation of Home Artificial Nutrition programs and that Home Parenteral Nutrition regulation has been issued earlier when compared to Home Enteral Nutrition (Moreno, 2001).

Within this topic, the Italian case should be highlighted since, in addition to national regulations for Home Artificial Nutrition, regional regulations are implemented, making even more difficult to have a legislative harmonization, even for the same country (SINPE, 2007). Despite legislative differences among countries, the funding for Home Artificial Nutrition is relatively uniform in Europe, with public health services supporting the costs of Home Parenteral Nutrition, and bearing totally or partially the costs of Home Enteral Nutrition (University of Bologna, 1995).
In Home Enteral Nutrition one point to be emphasized is the lack of general agreement in what is considered as Enteral Nutrition because, some countries include in this group oral feeding, such as enteral diets and nutritional supplements. In Italy, France and United Kingdom only tube feeding is considered as enteral nutrition, while in Austria and Croatia any enteral diet or supplement is classified as enteral nutrition. The majority of countries have a mix system, where a product is consider as Enteral Nutrition if complying with specific nutritional requirements (Moreno, 2001).

The first European legislation on Home Enteral Nutrition has been published in 1988 in Italy and France but some countries, in 1999, still didn’t have legislation (Moreno, 2001). In most European countries, hospital centers are responsible for implementation of HEN programs (Planas, 2002) but, in some countries, they still are limited to some centers. A general physician can, in most of the cases, prescribe Home Enteral Nutrition but preferably, it should be done by a Nutrition Support Team.

Costs can be supported partially or totally by National Health Services, while in other countries, patients have to fully support it (Moreno, 2001). A study collecting information about Home Enteral Nutrition in different European countries (Hebuterne, 2003), showed that, in Belgium, Denmark and Poland patients had to pay part or all of the charges, contrasting with countries like France, Germany, Italy, Spain and United Kingdom where costs are fully funding by respective government. Another conclusion of the same study states that home-made diets are being replaced by commercially available diets.

German reality on Home Enteral Nutrition showed around 100.000 ambulatory patients receiving reimbursed Enteral Nutrition, 30% of them in the home setting, 70% are tube fed for an average period of 9 months (Pahne, 2009). The reimbursement for Enteral Nutrition depends on medical prescription and is usually assured when normal food intake is impaired and modification of normal nutrition or other measures do not correct neither improve the nutritional status. There are no pre-defined diseases, clinical conditions or indications for reimbursement, neither list of recommended products; nevertheless composition criteria must be met. Price is usually set by manufacturing companies with total reimbursement, with the exception of patient contribution, set between 5 and 10 euros.
In Spain, the first legislation for Home Enteral Nutrition issued by the National Health Service was published in the late nineties, defining the clinical cases and indications for use, as well as the reimbursement system (Castaños, 2002). It was shown that different Spanish autonomic regions had different implementation methods and, in 2006, a new regulation was issued emphasizing that Home Enteral Nutrition should be prescribed by a nutrition specialist from a Nutrition Unit integrated in a hospital or other identity defined by autonomic region authority (Álvarez Hernández, 2008; García de Lorenzo, 2008). Nevertheless some uncertainties still go on when referring, for example, to the prescription of Oral Nutritional Supplements (Olveira, 2009). A clinical evaluation of the patient is required and some conditions have to be fulfilled: impossibility to cover nutritional requirements through regular ingestion, Quality of Life improvement with treatment, comply with sanitary requirements (like home cleanliness and existence of refrigerator) and not social criteria, tolerance to the prescribed enteral formula, benefits of nutritional support outweigh the risks, perform a periodic evaluation and clinical adjustment, if needed (Martínéz, 2004; Álvarez Hernández, 2008). Some clinical conditions are still not included in the approved list for HEN use and some logistic barriers still occur, as some Spanish regions do not accept prescriptions from other regions (García de Lorenzo, 2008). In Catalonia, is common the existence of agreements between hospital nutrition units and pharmaceutical industries for material and formula delivery and follow-up in patient’s home (Planas, 2002), while for example in Galicia, patients have to collect nutrition formulas and materials in hospital pharmacy (Villar Taibo, 2008). Home Enteral Nutrition programs in Spain include follow-up with regular visits (usually each 3 months), phone and written contacts, visits to primary care institution or nutrition units, but changes in clinical condition can promote plan adjustments (Álvarez Hernández, 2008). A few articles have assessed the use escalation of enteral nutrition products: in Madrid region, a follow up between 1998 and 2000 of Home Enteral Nutrition products sold in community pharmacies, shown an increase of packages selling by almost 43% and increase spending of 65% (Castaños, 2002), in Andalucia, the consumption of HEN products has increase from 1.3 million in 2000 to 37 million in 2007, representing 2.3% of expenditure on public prescriptions (Olveira, 2009). It is recognized that Home Enteral
Nutrition programs are not satisfactorily implemented in Spain, despite the expenditure on Home Enteral Nutrition products range between 2.7 and 3 million euros per year, corresponding roughly to 1 % to 1.5 % of pharmaceutical expenditure (García de Lorenzo, 2008).

In France, Home Enteral Nutrition is initially prescribed by specialized services in the hospital setting, but follow up might be performed either by the hospital or by private companies, according to a pre-established plan. Usually the hospital center is responsible for the first visit and, after it, patient should be visited each 3 months in the first year and each 6 months in incoming years (Crenn, 2014). This nutritional support is fully reimbursed by the social security, if needed for more than one month (Roberge, 2000).

Home Enteral Nutrition costs in Italy are fully funded and include home deliverance of nutritional products, syringes, infusion pumps and sets, and are performed according to a certified system (Paccagnella, 2008).

In the United Kingdom there is a well-organized home delivery system provided by enteral feeding companies or third party suppliers, to whom the National Health Service contracts the provision of this home care service. The care standards supplied by homcare companies are considered sophisticated and reliable, as confirmed by independent audits and customer satisfaction surveys (Russell, 2001).

Some concerns have been raised in the last years, and strengthened by the rise of the economic crisis, about the costs and benefits of Home Enteral Nutrition to healthcare systems. The widespread use with the associated escalating costs, led some private insurance companies and National Health Systems to reduce reimbursement or even not to initiate it. Eastern European countries such as Russia, Lithuania, Ukraine, Belarus, Latvia, and Estonia decided to not reimburse for HEN, on the other direction Poland has started Home Enteral Nutrition reimbursement in 2007 (Klek, 2014).

When compared with Home Enteral Nutrition, Home Parenteral Nutrition data and information is much more structured, associated to the fact of being a much more restricted therapy, with higher possibility of complication occurrence and with a higher cost.
Home Parenteral Nutrition regulation in Europe was first approved in 1975 in Denmark and for the great majority of countries, the National Health Service fully support the costs; in Germany costs can be shared with private insurances and in Israel all expenses are paid by private insurance companies (Moreno, 2001). In Europe, back in 1995, feeds and equipment for HPN were already supply by different entities: in some countries hospital pharmacies were the main responsible, in others commercial firms were dominant and others have similar distribution between both (University of Bologna, 1995).

Some countries restrict Home Parenteral Nutrition programs to certain hospitals and pre-defined specific diagnoses, and prescription criteria is much tighter since in some of the countries only hospital physicians or physicians from a Nutritional Support Team are allowed to prescribe this home nutritional therapy (Moreno, 2001).

In France a small group of dedicated centers, approved by an expert commission based on medical and pharmaceutical experience, were responsible for handling Home Parenteral Nutrition and to give support to hospital centers (University of Bologna, 1995; Moreno, 2001). This reality changed back in 2001 when liberalization was performed, allowing reimbursement of partial parenteral nutrition outside approved centers. Later on, Expert Centers composed by a multi-professional team including physicians, pharmacists, nurses and dietitians were created and became responsible for evaluating the need of Home Parenteral Nutrition for more than twelve weeks, allowing the home service to be provided by private entities (Crenn, 2014).

In Spain, Home Parenteral Nutrition in described in the legislative framework published in 2006 as one of the health programs supported by National Health System, but its implementation was not subject to further developed (Tejada Domínguez, 2011). Health care professionals, frequently integrated in clinical nutrition units, are responsible for HPN implementation, following the current guidance and applying their know-how (García de Lorenzo, 2008; Álvarez Hernández, 2008). HPN programs are supported by hospital centers, responsible for clinical evaluation and follow-up on a monthly basis (Álvarez Hernández, 2008) and a 2008 study focusing on the implementation of this nutritional therapy, show that in 713 Spanish hospitals, only 62 (8.7%) had HPN programs,
with more than 50% of this home service being provided by hospital centers and 17% by pharmaceutical infusion companies (Juana-Roa, 2011).

From the above described European reality, we can conclude that, in general, HPN programs are fully costed by the states, while for HEN, states can fully or partial support it, and in some cases not to reimburse it at all. Different national and regional regulation makes implementation, reimbursement and access widely different across Europe and the private sector is starting to have an increasing role in providing home care service. A statistically positive association has been found between the number of years since the first regulation and the prevalence of total HAN (SINPE, 2007).

United States

Unlike most European countries, where financing of Home Artificial Nutrition relies mostly on National Health Services, in the United States financing relies both on private insurance companies and governmental programs, such as Medicare or Medicaid (Moreno Villares, 2004).

Medicare is a federal health insurance program, established in 1965, covering individuals over 65 years old and those permanently disabled. It has a great importance in the health system being considered as a reference standard in many areas, with crucial influence in reimbursement policies for both public and private payers.

Medicaid provides also healthcare coverage for low income people in addition to elderly and disability coverage. It is administered together by the states and the federal government, organization that might lead to different coverage and required documentation among different states; for example, nearly all states require specific documentation of enteral therapy in the medical record (ADA, 2009; Parver, 2009).

In 1976 Medicare developed a reimbursement mechanism for Artificial Nutrition in non-hospital setting, followed by private insurances and Medicaid (Howard, 2000). This occurred when hospitals and insurance companies start to realize the financial benefits of early patient discharge to the home setting, leading to a vast development of home care
providers companies; both of these factors, help to explain the higher incidence of HAN in the United States when compared to other countries (Moreno, 2001).

Enteral Nutrition is considered as an effective and life sustaining therapy covered by public and private payers (Parver, 2009). There is some variation coverage and in some states Home Enteral Nutrition is covered by Medicare in almost 50% of patients, while in others, nearly 60% of HEN patients have private insurance coverage. Some insurance companies have their own specific criteria for eligibility and coverage but others follow general Medicare guidance. Either ways, it is very important to identify the type of coverage held by the patient and requirements specified by home care agency (Winkler and Albina, 2005), as the reimbursement process in the United States is very complex for both private insurances and public payers.

A few conditions should be met for Home Enteral Nutrition coverage by payers. For example, for Medicare coverage, beneficiary must have a permanent gastrointestinal track impairment, the nutritional support therapy should be reasonable and necessary to maintain (or increase) patient health status and needed for over 90 days (Newton, 2013). The primary diagnosis is also essential for coverage and there are four major indications for the approval of this nutritional support: impaired ingestion, impossibility to consume adequate oral nutrition, impaired digestion and absorption and severe nutrient wasting or growth retardation (Winkler and Albina, 2005).

Home Enteral Nutrition is usually not covered by Medicare when gastrointestinal track is functioning, unless in specific cases (like in patients with dysphagia who can swallow small amounts of food, or patient with Crohn’s disease requiring prolonged infusion of enteral nutrients due to malabsorption) that should be documented by the prescribing physician and accompanied by documentation from the patient’s medical record (Parver, 2009; Newton, 2013). Some situations are generally not covered for reimbursement, such as: oral feeding, patients in transition to an oral diet, patients that require only over-the-counter supplemental feeding, even if given by an enteral tube (Goff, 1998; Winkler and Albina, 2005; Parver, 2009).
If coverage is approved, *Medicare* pays 80%, with the remaining 20% to be supported by the patient itself or other secondary insurance, if available. Nevertheless, aside from HEN therapy, patients sometimes require additional services, like administration of antibiotics or oxygen that will rise the total cost to patient (Winkler and Albina, 2005; Newton, 2013); reimbursement limits also exist in nursing home care visits (usually 3 after hospital discharge) and nutrition professional visits are restricted to patients with other pathologies, like diabetes or kidney disease (Silver, 2004). Despite 75% of older adults on HEN rely on an informal caregiver, they are not included in *Medicare* coverage (Goff, 1998; Silver, 2004).

The home care service is usually provided by a supplier or home care company that accepts insurance company payment (Newton, 2013). Private payer negotiate reimbursement with suppliers of enteral nutrition by competitive bidding, giving in return a determined level of business and prompt payment to the home care provider company (Parver, 2009). Home care companies should have a significant knowledge in reimbursement mechanisms to ensure that they will be adequately paid for services delivered and, from a technical perspective, they must guarantee an adequate delivery system and a skilled clinical management (Ireton-Jones, 2002). Home care agencies can apply for certification by payers (for example *Medicare*), that will require adherence to federal demands for patient care and management (ADA, 1999); this certification might present a commercial advantage for agency selection, together with other features like experience on home care, flexibility, availability and consistency (Goff, 1998).

It is very important the creation of a nutritional plan, periodically revised according to clinical evolution. Other fundamental aspects for successful implementation are the formal training given to patient and their family (should be adapted to patient ability, knowledge and expectations), and the assessment of home conditions needed for nutritional program, like the existence of a refrigerator and running water, among others (Kovacevich, 2005).

Some concerns have been raised in the last years about the overuse of Enteral Nutrition, namely in the home care setting. One of the mentioned examples is the overuse of tube feeding in patients with advanced dementia, where existing data fail to
support improvement in survival, outcomes or functional status (Finucane, 2012). A tendency inversion in the use of Enteral Tube Feeding in patients with advanced dementia is already on the way, as revealed by a study performed in the United States between 1993 and 2004 that reported its decrease use since 1998 in this group of patients (Teno, 2008).

Measures to avoid the overuse and ensure the future of this nutritional support service are already under discussion, and proposals like modification of reimbursement schemes, increase competition between service suppliers and payment driven by performance (Parver, 2009; Finucane, 2012) are being considered. Thoughtful decisions on this issue should be made, because implementation of Medicare prospective payment system from 2000 onwards, has negatively affected the coverage of Home Enteral Nutrition in some population sectors, such as older adults, since follow up costs might outweigh the clinical benefits and, for this reason, some home care provider companies no longer provide this service (Silver, 2002).

As for Home Enteral Nutrition programs, to qualify to a Home Parenteral Nutrition program, several criteria must be met. A thorough review of diagnosis and other supporting documentation is performed and a correct flow of information between clinicians and staff responsible for verification and billing from the health care provider is essential (Hendrickson, 2013). Reimbursement of this home care therapy started after several academic centers in the United States reported a good rehabilitation of chronical intestinal failure with this nutritional support (Howard, 2006).

Coverage acceptance of Home Parenteral Nutrition is restricted to some clinical situations (for example, bowel resection or intestinal obstruction, inflammatory bowel disease, significant malabsorption and serious motility disorder) and when proved that Enteral Nutrition is not feasible or tolerated (Goff, 1998; Ireton-Jones, 2003). Patients must need the therapy over 90 days and should be evaluated within 30 days before HPN therapy initiation (Ireton-Jones, 2003).

HPN prescription is based on initial assessment of the clinical situation with the determination of the patient nutritional goals, requiring a careful planning and attention
to all details (Hendrickson, 2013). The home care provider is responsible for infusion bags and supplies delivery to the patient’s home and the service should include a 24 hour on-call clinical service, regular contacts, assistance in reimbursement and psychosocial support (Ireton-Jones, 2003).

Generally, Medicare will reimburse 80% of HPN therapy with the remaining 20% paid by secondary insurance or by the patient itself (Puntis, 1998; Howard, 2006; Hendrickson, 2013). Despite reimbursement of parenteral solution and infusion pumps, supplies and nursing visits, other cost might not be supported, like clinician monitoring time and extra supplies (Hendrickson, 2013). This may lead to an increase financial burden to patient and families, with caregivers being “forced” to keep their works, despite schedule adjustment and loosing opportunities for career progression (Winkler, 2006).

Brazil

In Brazil, Home Enteral Nutrition is regulated by federal districts that are responsible for defining the types of enteral nutrition, referral centers and treatment management. The hospital multidisciplinary team evaluates the clinical and nutritional status of the patient, planning the nutritional therapy and training for the patient and the family. The therapy is provided for free for all inhabitants, and it includes delivery of nutritional products and a follow-up made each 3 month to evaluate adherence, complications and illness (Zaban, 2010). Following publication of a decree regulating the supply of Home Enteral Nutrition in 2004, a study has been performed in order to evaluate the impact of regional regulation in prevalence and epidemiological data in one year period; a positive correlation was found between the regulation issuing and home enteral nutrition prevalence (Zaban, 2009).
Portugal

In Portugal, Home Artificial Nutrition is not regulated neither legislated and no national registry for Home Enteral or Parenteral Nutrition is available. This kind of databases, like NADYA in Spain and BANS in the United Kingdom, are very helpful from a clinical and epidemiological point of view, since they can be very helpful in establishing the status of therapy prevalence and implementation. In addition to this, no national clinical protocols are available leading to a variable implementation of this home care therapy and trusting the decision and application to each hospital center.

According to a Portuguese physician, Paulo Martins, Portugal is the only country from European Union without an implemented national program for Artificial Nutrition in ambulatory setting (LUSA, 2008). This program implementation would allow a global cost reduction for National Health Service, through two ways: reduction of hospital stay (with the consequent decrease of resource use and beds needs) and less re hospitalizations caused by infections, most of the times related with patient malnutrition; simultaneously it would increase patient Quality of Life. One of the measures proposed by the same physician was the creation of a reimbursement system for this type of nutrition, that should be available in community pharmacies.

A study performed in Portugal, evaluated the current nutrition practice, both in hospitals and in the primary care setting, through questionnaires completion sent by the Portuguese Association of Parenteral and Enteral Nutrition (APNEP) to all hospitals and primary care institutions (Ravasco, 2004). At the hospital setting, only 34 % of the total number of hospitals had reported the existence of a Nutrition Support Team and with a variable composition: none of them had a nurse and dietitians, nutritionists and pharmacists were the dominant health care professionals. Only 27 % of hospitals had educational nutrition programs and physicians were the main responsible for prescription and monitoring of oral, enteral and parenteral nutrition. Only 3, within 41 hospitals, identified the existence of a Home Artificial Nutrition Support Unit despite 11 of them (25%) reported to have patients receiving home enteral or parenteral nutrition. On the primary care setting, nurses are the most involved health care professionals and in 61% of
centers there were home care support teams, despite not specifically created for nutrition care. From the study collected data, Nutritional Support Teams are still not perceived as a key determinant factor for quality of care and there is a wrong perception of their mission, tasks and responsibilities. Nutrition teams still do not appear as multidisciplinary concept, and education and training need to be appropriately implemented.

A recent thesis published in 2012 (Moreira, 2012) has showed some of the current practice of Home Artificial Nutrition in Portugal. Two hospitals have shared their experience on this topic - Hospital Garcia da Horta and Hospital Distrital de Faro – and a brief description is presented hereafter.

**Hospital Garcia da Horta**

An Enteral Nutrition Group has been created in 1999 in this hospital, following currently around 120 - 150 patients on Home Enteral Nutrition. The process starts with access insertion and a thigh control made in until the sixth month. After this, a regular follow-up is made when the patient goes to the hospital to routine consultation and to receive the materials needed for Home Enteral Nutrition. No home nutrition scheme (including material delivery, routine medical visits, follow-up at patient home) is implemented for artificial nutrition. Average duration for Home Enteral Nutrition treatment is around 24 months but it can range from a couple of months to eight years. Regarding Home Parenteral Nutrition program, no patient is at the moment receiving this therapy in the hospital; over the last 8 years, eleven patients were treated with an average duration of 39 days.

**Hospital Distrital de Faro**

This hospital presents currently a partnership with a pharmaceutical company, following roughly 10 to 20 patients on Home Enteral Nutrition. The pharmaceutical company is responsible for the follow up of patients that includes two weekly visits, a
permanent phone contact (24 hours, seven days a week) for patient support, periodic training and the for home delivery of enteral formulas and other support materials. The nutrition support team (composed by a nurse and dietitian) are contractually part of the pharmaceutical company, despite working close together with the hospital. It is hospital responsibility to evaluate and identify patients that need this therapy and then inform the company.

In order to evaluate the implementation and outcomes of Home Enteral Nutrition program, the hospital itself has evaluated this nutritional therapy between the years of 1996 and 2006. In respect to the patients enrolled in the program, the mean age was 59 years, most of them were at home and only a small percentage in other care facilities, 37% of patients were independent, the main underlying diseases were neurologic and oncologic and the average treatment length was 7.6 months. In the outcomes, the number of patient re-hospitalizations has calculated before and during Home Enteral Nutrition program; before nutrition support, patients had an average of 2.2 re-hospitalizations per year (with an average of 46.8 days per hospitalization) and during Home Enteral Nutrition program it has been reduced to 1 re-hospitalization per year (with an average of 7.9 days per hospitalization).

The hospital evaluation for the therapy was very positive, due to the reduction of mortality and morbidity, reduction of number and duration of re-hospitalizations (with consequent reduction of direct and indirect costs) and increase of patient Quality of Life due to integration in family and society (Moreira, 2012).

The lack of a legislative framework in Portugal leads to a differentiate access of the population to HAN programs and hospital centers are normally responsible for their implementation. A few milestones can help in developing this nutrition support therapy: the creation of nutrition working groups in hospitals to support Home Artificial Nutrition implementation, increase availability of nutrition professionals and a better coordination between hospital and community.
CHAPTER VI - Costs and Benefits of Home Artificial Nutrition

Economic evaluations: brief definition

Economic evaluations can be defined as a comparative analysis of costs and consequences between two (or more) alternative health care technologies. In order to make this comparison, identification and measuring of both costs and consequences ought to be performed.

Economic evaluations are becoming widely spread and are recognized as a key factor in the decision making process, both for medicines and other health care technologies (Pritchard, 2006). The objective of health economics is to maximize population well-being with the available (and most of the times scarce) resources, using them in a wise and appropriately manner (Russell, 2007; Olveira, 2009); this is crucial for payers and policy makers, namely in times of budget restrictions. This assessment is even more important due to the large (and potentially infinite) demands in health systems and the ethical implications that this kind of decisions might have to populations (Olveira, 2009). Health care therapies supported (totally or partially) by National Health Services or private insurances should prove their “value for money” and payers should evaluate the additional clinical benefits and the health care costs of the new intervention when compared to the standard one (Walzer, March 2014).

Four methods can be used to evaluate the efficiency of a particular medicine or any other healthcare technology (Richards, 1996; Cade, 1997; Puntis, 1998; Waitzberg, 2007; Olveira 2009):

- Cost minimization: when the alternatives under comparison have the same proven effectiveness or similar results, the one with the lower total cost (monetary values) would be the more efficient one.
- Cost effectiveness: the outcomes of the new technology are presented in the same natural units for both alternatives (for example years of life gain, number of lives saved, number of complications avoided, number of hospitalization days reduced) and costs on monetary values. While the outcomes
of both alternatives are of the same type, their magnitude may vary. In this case, an incremental cost-effectiveness ratio (ICER) is usually calculated, showing the cost of each additional unit of effectiveness.

- Cost utility: in this complex method, the outcomes or benefits of the treatment might be different and more than one since what is being compared is the patient utility gain. The utility gained through a health status improvement is usually measured in Quality Adjusted Life Years (QALYs), combining in a single unit survival and Quality of Life (QoL). The consumed resources are converted into the monetary equivalent allowing the comparison of different treatments on the basis of the marginal cost (cost to treat one additional patient) per Quality Adjusted Life Years gained. This economic tool is useful for compare different treatments for the same condition and is frequently used (and recommended) by National Institute for Health and Clinical Excellence (NICE) from the United Kingdom, for clinical practice guidance.

- Cost benefit: this analysis puts monetary values both on benefits and costs. Monetary value can be used to measure benefits not only from the patient point of view, but also in a wider range (social or economic) such as other groups or individuals affected by patients. It is a measure of financial return on investment in a given health care program.

Measuring the outcomes and benefits of health care technologies can be done, as mentioned above, in different ways: by natural units, monetary values (allowing a wider evaluation of benefits, for example for caregivers or society) or utility gain, usually measured by Quality Adjusted Life Years (QALYs) that combines both survival and Quality of Life.

Quality of Life is a multidimensional concept that describes health status in diverse areas, such as physical, physiological, social and somatic domains of functioning and well-being (Baxter, 2006). Referring to Home Artificial Nutrition, there are a few instruments frequently used in assessing patient Quality of Life: general measure instruments, such as Short Form 36 Questionnaire (SF-36), Quality of Life Index (QLI), EuroQol 5D (EQ-5D), Sickness Impact Profile (SIP) and Nottingham Health Profile (NHP)
and disease specific questionnaires like *Inflammatory Bowel Disease Questionnaire* (IBDQ), *European Organization for Research and Treatment of Cancer* (EORTC) core questionnaire, supplemented by disease-specific modules (Winkler, 2005; Baxter, 2006). Quality of Life is better assessed by self-rating, since it relies in individuals subjective perception that are, in some cases, almost impossible to determine by other person; nevertheless, proxy rating is also very important because in some cases, patients are in a non-consciousness state (Loeser, 2003).

Three other concepts are important for performing an economic evaluation for health care technologies: the comparator establishment, the discounting and willingness-to-pay threshold. While evaluating a new technology, it is very important the definition of the current practice to be considered in the evaluation, since this choice will influence greatly the obtained results. Discounting consists in converting costs and benefits that would occur in the future to equivalent present values (Cade, 1997) and usually ranges from 3% to 6%, according to each country. Willingness-to-pay threshold (or critical rate) is the amount that a society or health care system is willing to pay for each additional life year or Quality Adjusted Life Year gained with the new intervention when compared with standard one. It is represented by the maximum acceptable Incremental Cost Effectiveness Ratio (ICER) and this threshold varies from country to country, in the United Kingdom an implicit willingness-to-pay threshold of 30,000 pounds per QALY is usually applied (Walzer, May 2014).

**Economic evaluations in HAN**

The importance of medical nutrition has been increasingly recognized by health care decision makers, since it is widely accepted that an adequate nutrition status in the community setting improves global health of the population contributing, this way, to the sustainability of health care systems (Walzer, May 2014).

Despite proven efficacy and cost-effectiveness in different health care settings, some concerns have been raised about the lack of health related economic data for medical nutrition and nutrition “value for money” evidence is less common, even if levels
of prescription to patients and reimbursement policies are assured by health care systems. This situation is divergent in respect to medicinal products and some medical devices, where economic evaluation has been developed and proven for many years. Health economic evidence for medical nutrition interventions is scarce, few economic evaluation articles exist and willing to pay threshold is rarely applied; one of the reasons might be that, until recently, they have not been required for reimbursement or coverage decisions (Olveira, 2009; Walzer, March 2014; Walzer, May 2014). Nutritional therapy interventions are usually integrated in other healthcare processes, such as the recovery after surgery, making very difficult to isolate and evaluate the nutritional effect; for this reason, some authors refer that nutrition should be seen as a sole category within the global health care reimbursement system (Walzer, May 2014). Other reasons identified for the lack of economic data for medical nutrition in the home setting, is the complexity to perform studies outside the hospital controlled environment and the difficulty to establish a definite connection that changes in Quality of Life verified are due to nutritional support implementation, rather than the natural course of the underlying disease.

Another point to be discussed is what to consider as the standard / current therapy. In the case of a new alternative is being proposed (a home care program in this case), to what alternative should it be compared: doing nothing or hospitalization? Since in most of the times a randomized trial is not feasible, authors might consider a theoretical hypothesis (what would happened) or a retrospectively analysis (what had happened prior to implementation of the new therapy) (Cade, 1997). The alternative selection is also very important when evaluating the outcomes and the Quality of Life. As an example, it would not make sense to compare in a direct way the Quality of Life (or other parameter, like survival or functional capacity) of a patient undergoing Home Parenteral Nutrition, usually reported to be low, with the average values for the general population, due to its impact on daily activities (Detsky, 1986), catheter-related complications, technological challenges, decreased social activity, impact on family relationships and friendships, depression and financial burden (Winkler, 2014).
Measuring Quality of Life in Home Artificial Nutrition patients can involve assessment made by patient itself, close family member or caregiver and healthcare professionals (Howard, 2006); although patient rating is the preferred one, sometimes is not possible to perform it, due to patient coma or dementia situations. Some authors also claim that caregivers should evaluate their own Quality of Life, since complex home care therapies (like Home Parenteral Nutrition), need significant training in order to support the patient, is very time-consuming and brings schedule constrains, impacting daily life and familial routines.

Quality of Life describes a patient’s subjective experience and obtained results depend not only from the nutritional support implementation itself, but from the prognosis of the underlying disease (including frequency, magnitude and duration of symptoms), patient emotional characteristics and perception of her/his own health and family support (Roberge, 2000; Winkler, 2005). HAN programs are recognized has having significant impact on Quality of Life of patients and their families due to its influence on daily routine, work environment, financial well-being and independence (Baxter, 2006). The impact can be so substantial that some authors even consider Home Parenteral Nutrition as a treatment of a disease complication rather than a disease treatment (Howard, 2006). Generic tools for measuring Quality of Life are not optimal since they do not distinguish effects from underlying disease and those from the nutritional support (Staun, 2009) but, the use of specific instruments for chronic diseases might also present some challenges that would result in lower scores for patients on HAN (when compared with those with the same clinical condition but without nutritional support), namely if the implementation was due to an acute life changing event (Howard, 2006). For example, for a patient with an acute clinical situation starting on a Home Parenteral Nutrition program, a sudden fall on Quality of Life is verified; in opposition, a patient with multiple operations and hospital admissions, the implementation of this home care support might mean an increase on its Quality of Life (Baxter, 2006). Within Home Artificial Nutrition, Home Parenteral Nutrition is considered as the therapy with more impact on patient’s Quality of Life, presenting lower values when compared with general population QoL. Impact on sleeping, travel, leisure activities, social life, joy, financial implications and
decreased physical and performance status have been frequently described in several studies for HPN patients (Winkler, 2005; Baxter, 2006).

The methods used to assess benefits in Home Artificial Nutrition studies are very diverse and usually adjusted to the available data, resulting in the use different scales, instruments and domains to access the Quality of life in patients, making very difficult to compare outcomes between different studies. Benefits frequently listed in the HAN evaluations are Quality of Life improvement, morbidity and mortality, physiological and psychological complains, hospitalization length, social rehabilitation, among others (Pironi, 1995). According to the type of nutritional support implemented, additional parameters and outcomes (to those mentioned above) are evaluated. In Oral nutritional supplements and Enteral tube feeding it is frequent the control of body weight and nutritional intake, muscle strength, activities of daily living, immunological parameters, fatigue level, wound healing and prevention of pressure ulcers as well as other functional improvements (Stratton, 2006).

Globally, studies present better results on patients with chronic conditions (such as Crohn's disease or motility disorders) when compared with oncologic patients; age also plays an important role, with younger patients with better results, but age itself should not be an eliminating factor (Howard, 1995; Moreno Villares, 2004). Self-esteem and good family support are critical for successful program implementation, attenuating patient impact on employment, income and decreased social interaction (Howard, 2006). Results from such evaluations should be used to highlight areas where interventions are more cost-effective and those where interventions less cost-effective.

Costs can be roughly divided in three major categories (Olveira, 2009):

- Direct costs including hospital expenses (on acute or long term care hospital facilities, geriatric residences), medical consultations, home care assistance, medicinal products, nutritional formulation, labor, wages, training of patients and family, laboratory tests, among others. This kind of data is easily collected and appears in most of the studies.
Indirect costs including productivity losses caused by associated diseases, early retirement and early mortality. The vast majority of studies in clinical nutrition do not include these type of costs for two reasons: difficulty to assign monetary values to this kind of parameters and many patients that need home artificial nutrition have severe clinical conditions and/or are older adults where the possibility to return to an active professional situation is somehow reduced.

Intangible costs (such as pain or dramatic changes in lifestyle) are usually not considered due to the difficulty to match these parameters to monetary values.

It has been mentioned that costs in Home Artificial Nutrition are more expensive in the United States of America (Pironi, 1995) and Home Enteral Nutrition is likely to be nine times less expensive when compared with Home Parenteral Nutrition (Pironi, 1995; Kovacevich, 2005; Paccagnella, 2008). The majority of studies in HAN calculate costs from the payer / health care provider perspective, and only some of them consider the costs supported directly by patients and their families, the Out of Pocket expenses.

One of the most frequent underlying diseases leading to nutritional support therapy (Home Enteral or Parenteral Nutrition) is cancer that, itself, has a significant impact in all dimensions of patient life, from psychological to physical functions and social well-being. Nutritional status is affected by this complex pathology in several ways: introduction of a pharmacological treatment, metabolic changes, lower food intake and increasing waste; for this reason nutritional follow-up should be present in all stages of the disease and considered part of the therapeutic strategy (Caro, 2007). Nutrition support in patients with late stage cancer is controversial, since the major determinant for the outcomes is the oncological disease rather than the nutritional status (Bozzetti, 1997), but studies point toward increased tolerance to treatment, decrease rate of complications and optimization of balance between energy expenditure and food intake provided by this support (Caro, 2007).

Despite no sufficient quality studies are available, it is generally considered beneficial to implement nutritional support, such as Home Parenteral Nutrition, when
death by starvation would precede death from the underlying disease and life expectancy is likely to be over 2 months (Bozzetti, 1997; Muscaritoli, 2013), but the decision should be taken on a case-by-case basis, considering the risks and benefits of therapy implementation (Orrevall, 2013). In Sweden, Home Parenteral Nutrition is much more common than Home Enteral Nutrition in palliative cancer, even in cases where oral food intake is available and patients have a functional gastro intestinal track (Orrevall, 2009).

**Costs studies**

When performing a health economic study, costs associated to the different alternatives under evaluation should be carefully collected and evaluated. In the following paragraphs we will focus our attention on references and articles that evaluated costs of Home Artificial Nutrition program implementation, in several countries around the world.

Costs obtained in the literature review differ significantly between them for a few reasons: type of nutritional support under evaluation, different country reality (and associated life cost), year of article publication and types of costs included in the study.

In general, it is accepted that Home Artificial Nutrition programs (including costs for nutrition formulas, associated equipment, health professional home visits, among others) represent a cost reduction of between 60 and 70%, when compared with hospital inpatients, with a great share of savings arising from the avoided hospital costs (Planas, 2002). For Home Parenteral Nutrition, cost reduction when compared to Parenteral nutrition in the hospital setting ranges from 25% - 50% (Puntis, 1998) to 30%-60% (Howard, 2006). As mentioned above, Home Enteral Nutrition costs are assumed to be one tenth of those of Home Parenteral Nutrition. In the United States, between 1989 and 1992, *Medicare* beneficiaries on Home Enteral or Parenteral Nutrition had increase on 25% both in use and cost, leading to a total cost of 1.6 billion dollars in 1992, when considering only direct costs and excluding laboratory monitoring, health care professional visits and re-hospitalizations (Howard, 2000).
Home Parenteral Nutrition is considered an expensive therapy and estimations point to yearly costs of around 140,000 dollars in the United States for 1992 (Hendrickson, 2013), ranging between 150,000 and 250,000 dollars in the United States and around 55,000 pounds in the United Kingdom in the mid-nineties (Puntis, 1998). For the year 2000, yearly costs per patient with Home Parenteral Nutrition were estimated to be 60,000 pounds in the United Kingdom and between 60,000 and 250,000 dollars in the United States, when considering nutrients, pumps and disposable equipment (Colomb, 2000). Based on Medicare and Medicaid reports, annual reimbursements for healthcare professionals range from 100,000 to 250,000 US dollars per patient on HPN, plus 10,000 to 196,000 US dollars for HPN related hospitalizations (Piamjariyakul, August 2010).

Some studies have focused their attention on HPN costs in several countries around the world: in Switzerland a mean monthly cost of 2,900 Swiss Francs for Home Parenteral Nutrition has been reported (Shaw, 2013) and in New Zealand costs were estimated to be 76,000 Australian dollars per patient for 2006 (Gillanders, 2008).

In France, an assessment of Home Parenteral Nutrition costs in two approved French centers - Montpellier and Strasbourg - has been performed with data collected in 2002 and 2003 (Aatmani, 2006). This study had only considered directs costs, excluding the indirect ones (like unemployment) and costs associated to complications and re-hospitalizations; the method for data collection was a questionnaire filled by 22 patients and nurses, complemented by data from dispensary, financial administration and different organizations. The expenses included medicinal products, materials and respective maintenance, product transportation to the home setting, laboratory tests, patient transportation and healthcare personnel, calculated according to the national health insurance fund and hospitalization prices for 2003, in France. Obtained results show an average cost of 30,232 euros per patient per year (i.e. 2,519 euros per month and 83 euros per day), with medical costs (personnel, nutrition bags, material, laboratory tests) accounting for more than 90 % of total costs. Technical equipment and nutrition bags account for 58 % of costs, followed by expenditures on hospital and non-institutional personnel (16 % each). The great majority of expenditure, almost 80% (equivalent to 65 euros per patient per day), were assured by the institution’s global budget (including
personnel, nutrition bags, material, home delivery) and the remaining by the Health Insurance Fund (22% of overall costs, corresponding to 18 euros per patient per day).

Another approach to evaluate the costs of Home Parenteral Nutrition is to compare it with hospital Parenteral Nutrition. This analysis performed between 1996 and 2001 in Ontario, Canada (Marshall, 2005), consisted in a retrospective cohort with 29 patients transferred from hospital to home (keeping their parenteral nutrition) from the perspective the Canadian government provider. Average daily direct medical costs were estimated for the 2 last weeks before patient discharge from hospital and on the first month after discharge. In the hospital setting the following expenses were considered: hospital hotel costs, medicinal products and intravenous solutions, clinical procedures and tests, laboratory analysis and transfusion services, physician fees; for patients in the home setting, costs considered were: medication profile consumption established based on discharge review, consumption of acute care resources (including hospital readmissions and emergency room visits), contracted services (such as nursing, occupational therapy, physiotherapy and nutrition), estimated from patient specific home care invoices. Average daily costs in the home setting were roughly 30% less than in-hospital patients subject to Parenteral Nutrition treatment. During the first month after discharge, net savings per patient were estimated to be 4860 Canadian dollars, increasing to values of 5400 among those with underlying malignancy and 7170 for patients over 55 years old. This study showed that Home Parenteral Nutrition program implementation is a cost saving therapy, when compared with hospital setting, and higher savings were obtained in older patients and those with active cancer. The authors identify some weak points in the article such as the low number of patients, short time horizon analysis and the non-inclusion of indirect or private payer costs.

One situation frequently discussed, namely in the United States where Home Parenteral Nutrition programs are not fully supported by the payers, is the fact that reimbursement systems (either assured by public or private payers) might not cover all expenses that arise from this nutritional support. The economic impact in families that access Home Parenteral Nutrition might lead to financial strains, and only a few studies reflect this effect, since the great majority of studies only consider costs from the payer
perspective, through provider billing and reimbursement information (Gaskamp, 2004). In the United Stated, a study had its focus on non-reimbursed cost supported by families, using questionnaires and semi-structured interviews in a sample of 80 families (Piamjariyakul, September 2010). On average, families on Home Parenteral Nutrition, pay almost 18,000 dollars per year in out-of-pocket expenses. Considering other non-reimbursed billing costs in health service and one hospitalization, estimated to be around 13,000 dollars, the total annual costs for a family with a patient on Home Parenteral Nutrition may go over 30,000 dollars even with insurance coverage, rising some ethical concerns about the accessibility of this nutritional therapy to all population. Financial constraints associated with wage losses due to decrease employment, large out-of-pocket expenses and non-reimbursed payments, decrease in insurance coverage and inability to pay monthly bills is associated with feelings of depression, affecting patient Quality of Life (Gaskamp, 2004; Winkler, 2014). A Canadian study found that low-income patients had significantly greater catheter sepsis rates when compared with those with average or high incomes (Winkler, 2014). Other additional costs occur within the family setting usually not accounted for, such as, missed work to accompany HPN patient to clinical follow-up or job loss due to permanent supervision needed for the patient (Howard, 2006); expenses arising from therapy complications (like renal, gastro-intestinal, metabolic, bone related, hepatic and biliary diseases) should also be taken into account, as well as additional fees for its treatment (Winkler, 2014).

Home Enteral Nutrition costs were estimated, by the largest payer, to be around 137 million dollars, in 1992 for the United States (Williams, 1998). At the end of the nineties, a study followed 1397 patients starting Home Enteral Nutrition in several European countries, calculating the expenses of this therapy (Hebuterne, 2003). Costs considered were due to nutritional formulas, infusion pumps, micronutrients and related equipment (bags, tubing and dressings), while costs associated to caregiver, re-hospitalizations and medical monitoring were not included. Daily overall costs found of Home Enteral Nutrition were around 12 euros in Belgium, 10 euros in France, 23 euros in Germany, 24 euros in Italy, 12 euros in Poland and 17 euros in Spain.
More recent data has been collected about the costs of Home Enteral Nutrition in several countries: in the Spanish region Galicia a retrospective review made with 237 patients had calculated a monthly mean cost of 160 euros (Villar Taibo, 2008), in Switzerland a mean monthly cost of 225 Swiss Francs for Oral Nutritional Supplements and 1447 Swiss Francs for Home Enteral Nutrition has been reported (Shaw, 2013), and in Germany average costs per month and per patient, range between 580 and 650 euros (Pahne, 2009).

As occurring for Home Parenteral Nutrition, studies have compared cost of Enteral Nutrition at home and at the hospital setting. A study published for a federal region in Brazil (Zaban, 2009) showed that annual expenses in 2005 range from an average of 19.000 euros for Home Enteral Nutrition to an average of 50.000 euros for Enteral Nutrition at the hospital. The costs for Enteral Nutrition in the hospital were 2.65 higher than the same program at home and included non-medical costs (such as health professionals involved in manipulation, delivery and administration of products, installation costs like water and energy) in addition direct costs of the product and infusion sets.

In Japan, a long term care insurance plan has been established in 2000 to support patients on Home Artificial Nutrition and cost supported by each family range between 300 and 400 dollars per month, value that according to study authors, might encourage its use and promote the overuse (Shintani, 2013).

Benefits studies

In order to evaluate the effectiveness of a new health technology, outcomes and benefits of alternative programs must be measured. Home Artificial Nutrition studies present a variety of items considered as outcomes, some of them associated with nutrition status, for instance weight maintenance and biochemical and anthropometric parameters. Commonly, when implementing a new health care technology, there is an association between long survival and rehabilitation but this situation might not occur in HAN programs, for example in clinical situations like severe intestinal or swallowing...
diseases, neurological diseases or stroke (Howard, 2000), where the main goal is to keep patient’s health and nutritional status.

Two factors have a significant influence in the outcomes of HAN program implementation: underlying disease and age. The underlying disease has influence on symptoms, physical function, general health and global Quality of Life (Winkler, 2006) while, referring to age, younger patients (namely for HPN) have better outcomes and survival after therapy implementation than older ones. Elderly present more medical fragility and less ability to cope with gastro-intestinal disabilities (Howard, 2006), but age itself should not be an excluding factor for therapy implementation in older people, both for Home Enteral Nutrition and Home Parenteral Nutrition.

The impact of Home Artificial Nutrition on Quality of Life depends also on the patient clinical history. For a patient with a chronic disease and multiple hospitalizations, nutritional therapy implementation (namely in Home Parenteral Nutrition) might represent an increase on Quality of Life, in opposition to patients undergoing nutritional support due to an acute situation (Staun, 2009). Other parameters influencing the patient Quality of Life are: clinical effects (complications and side effects, sleep and fatigue, depression, body image), social effects (lack of social activity and dynamics, isolation) and economic effects (decrease rate of employment, insurance and coverage restrains, Out of Pocket expenses) (Winkler, 2014). Handling with complex and advanced medical devices needed for Home Artificial Nutrition programs might, itself, influence negatively patient Quality of Life (Winkler, 2006).

As mentioned above, some questions have been raised about the use and benefits of Home Artificial Nutrition in cancer patients. The most determinant factor in cancer patient outcomes is oncologic disease, despite benefit recognition of HAN in patients with malnutrition arising from reduce food intake and cancer treatments (Muscaritoli, 2013; Culine, 2014; Senesse, 2014). The majority of Home Artificial Nutrition studies show that in cancer patients who survive for a few months only, Quality of Life gain is modest, namely when compared with patient with a non-malignant disease (Bozzetti, 1997) and for patients with very low nutritional status, advanced anorexia and
life expectancy lower than 2 months, benefits are considered reduced or even null (Muscaritoli, 2013). A study in Italy (Bozzetti, 2002) has prospectively followed 69 patients with incurable cancer on Home Parenteral Nutrition and Quality of Life was assessed using the Rotterdam Symptoms Checklist (RSCL) questionnaire (validated for Italian population) filled by the patients at therapy start and in a monthly basis at home. Median survival was 4 months, nutritional indices have been kept and Quality of life had remained stable until 2 or 3 months prior to death, showing that this home care therapy might benefit a percentage of patients who survive longer than the estimated time for starvation and clinical depletion, usually 3 months. Another study in Sweden (Orrevall, 2013) has collected data of 1083 patients with cancer, the great majority in palliative home care services, with 11% of total patients undergoing nutrition support through Enteral Tube Feeding or Parenteral Nutrition. Registered nurse/physician who followed these patients, report that Enteral Tube Feeding treatment was beneficial for almost all patients, while in Parenteral Nutrition had benefits in three quarters of patients and should be recommended for patients with more of 2-3 months of expected lifetime. A more recent study (Vashi, 2014) had investigated the Quality of Life and nutritional outcomes for Home Parenteral Nutrition in patients with advanced cancer. It consisted in a longitudinal non-randomized clinical study, following 52 adults with advanced cancer (average age of 53 years) treated at an oncologic center in the United States, from April 2009 and November 2011 followed until March 2014. Patients were evaluated at baseline and every month while on Home Parenteral Nutrition, and the instrument used for Quality of Life assessment was the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30). For nutritional and functional status appraisal, two instruments were used: Karnofsky Performance Status (KPS) and Subjective Global Assessment (SGA), both of them replied by health care professionals. Obtained results show improvement on nutritional and functional status after the first month and on Quality of Life patient after the second month, despite overall survival stayed just above 5 months. Home Parenteral Nutrition is associated with increased Quality of Life and nutritional/ functional status in advanced cancer patients despite of the type of tumor, namely after 3 months of nutritional support.
The conclusions mentioned in the above studies are in line with ESPEN guidance that do not recommend nutritional support program, in the case for Home Parenteral Nutrition, for patients with both incurable diseases and short life expectancy (Staun, 2009).

Several studies have been published focusing on the benefits and outcomes of Home Parenteral Nutrition, evaluating this nutritional support associated with the underlying disease.

One study centered its attention on the assessment of the Quality of Life in patients with intestinal failure receiving Home Parenteral Nutrition (Richards, 1997). 51 patients with intestinal failure were enrolled, with an average age of 44 years old and a median duration on HPN of 4 years. The Quality of Life was measured using two validated instruments: Short Form (SF) 36 health status questionnaire (United Kingdom version), that examine eight aspects of life domains, scoring each of them on a scale from 0 to 100% and EuroQol to obtain utility scores for a health status on a scale from zero to one, where zero corresponds to death and one to best possible Quality of Life. Results for both instruments were similar and, as expected, scores for physical function and role, pain, vitality, emotional role and social function on these patients were significantly lower than normal population scores. Younger patients (less than 45 years) had better results, approaching to those of normal population in most of domains tested, while older patients had the poorest results. 80% of patients reported to be too ill for work and only 10% were working full time or studying. Results show that patients undergoing Home Parenteral Nutrition have, on average, a fairly good Quality of Life and, due to the lack of available alternatives, this option seems to be acceptable.

To appraise Quality of Life and other dimensions related to physical and functional well-being, social/family and emotional well-being, 50 patients receiving long term Home Parenteral Nutrition in Israel have been enrolled to reply to Functional Assessment of Anorexia/Cachexia Therapy (FAACT) questionnaire (Oz, 2008). The mean age of patients was 31 years old, median length for Home Parenteral Nutrition was 27.5 months and less than 10 % of patients had active cancer. The response could vary from
grade 0 (corresponding to no acceptance) to grade 4 (full acceptance) and results range from 1.77 in physical activity, 1.8 in emotional status, 1.95 in oral intake until 3.18 in social activity. The relatively high grades obtained may be associated with the low patient age and low incidence of oncologic condition; despite this only a minority of patients had an active professional life.

A study published in 2014 (Culine, 2014) had assessed the impact of Home Parenteral Nutrition on Quality of Life for French patients with heterogeneous cancer. It consisted in an observational prospective study in adult population performed between 2009 and 2010, where physicians, patients and family members were asked to fill in a questionnaire before HPN administration and 28 days after. For Quality of Life evaluation, a self-administered questionnaire - Functional Assessment of Cancer Therapy – General has been used. From 767 patients initially included, 437 ended the study, with a mean age of 63 years, where gastrointestinal cancer was reported in 50% of patients and malnutrition was identified on almost 99% of patients. After 28 days of Home Parenteral Nutrition implementation, mean weight increase by 2.5%, and all sub-scores of Quality of Life have improved: mean physical well-being by 13 %, familial/social well-being by 3.2 %, emotional well-being by 4.1% and functional well-being by 6.6 %. General Quality of Life has improved in 60 % of patients, 15 % had a stable value and 25 % of patients had a decreased score. Almost 80% of patients had a positive perception of the impact of this nutritional support implementation, in line with the feedback from family members and physicians. Even though, authors underline the importance of randomized controlled studies to confirm the results, emphasizing that 28 days is a short period of time for outcome evaluation. With the data obtained from the above mentioned study (Culine, 2014), a specific analysis has been performed for one patient sub-group: 370 patients with gastrointestinal cancer (Senesse, 2014). Of these, 71% had metastasis, one third was over 70 years old and undernutrition was reported in over 90% of patients. Results after 28 days on parenteral intake show a global increase on patient Quality of Life, weight enhanced by 2.7%, a reduced nutritional risk and better overall results on patients receiving nutritional therapy overnight only. On the other hand, no significant upgrade
was reported in social, emotional and functional well-being. Family recognizes its benefits, despite lower perception of well-being when compared to patient itself.

In the literature review, a reasonable amount of benefit studies for Home Enteral Nutrition have also been found.

A study published in 2000 followed 38 patients (24 men and 14 women) on Home Enteral Nutrition between 1997 and 1999 in a French center, with an average age of 56 years old (Schneider, 2000). It intend to evaluate Quality of Life on long term Home Enteral Nutrition patients through two self-administered validated, non-disease specific and health-related questionnaires: Short Form-36 questionnaire (SF-36) and EuroQol that comprises EQ-5D index and visual analogue scale. For 14 patients not able to understand or reply to questions (due to neurological disorders or decreased consciousness) a subjective not validated assessment questionnaire was created based on author clinical experience and replied by a close relative. An increase in mean body mass index has been reported, after an average duration of 25 months on Home Enteral Nutrition. Result analysis revealed poorer quality of life parameters in comparison to a general population, with better results obtained for younger patients (under 45 years old), patients without cancer and with more than one caregiver. Even so, patient subjective assessment on Quality of Life since the beginning of Home Enteral Nutrition was generally good, with most patients reporting improved mental and physical well-being.

A study performed in France (Roberge, 2000) focus its attention on Quality of Life in patients with head, neck or esophageal cancer that undergo Home Enteral Tube Feeding. This prospective study was conducted from January till July 1997, evaluating the impact on Quality of Life in 39 consecutive patients (mean age of 58 years old) at a French center. This evaluation was made through several self-administered questionnaires: European Organization for Research and Treatment of Cancer (EORTC QLQ-C30) to appreciate generic quality of life data and validated for French language, complemented by two other disease specific questionnaires (EORTC H&N35 for head and neck cancer and EORTC OES24 for esophageal cancer). In addition to the mentioned questionnaires, a new one was developed to appraise Home Enteral Tube Feeding tolerance and tested.
prior to the study in ten patients. Evaluations were made after hospital discharge and 3 weeks later and results show a slight increase in global health status and Quality of Life. Some symptoms scores had improved expressively namely constipation, coughing, social functioning and body image, but patients still reported some difficulties in family and social life, indicating the need of psychological support after hospital discharge. The study has evaluated a low number of patients and during a short period of time. Another French study published in 2001 (Schneider, 2001) has analyzed prospectively one month mortality and long-term outcomes of home enteral nutrition. Between 1990 and 1996, 417 patients with a mean age of 64 years were enrolled for this assessment with a mean duration of Home Enteral Nutrition around 242 days. Probability of being alive after 1 month was 80%, after 1 year was 42% and after 5 years was 25%. Poor outcomes were, according to authors, due to disease severity with worse prognosis identified in patients with dementia, neurologic disease, head and neck cancer, Acquired Immune Deficiency Syndrome (AIDS) and in patients over 70 years old. Benefits were found to be more pronounced in patients returning to full oral nutrition, highlighting the importance of an accurate patient selection.

Other work proposed to evaluate the association between nutritional status and Quality of Life (Loeser, 2003), in patients with Home Enteral Nutrition through a tube feeding. This study consisted in a prospective cross-sectional study in 155 consecutive patients, and from these group, 56 patients were enrolled for a prospective longitudinal study with a 4 months follow-up. Patients and/or close relatives were interviewed, clinical information (like disease history and symptoms, weight changes) assessed and data collected between 1997 and 1999. The Quality of Life has been evaluated by proxy rating (Karnofsky and Spitzer indices) and self-rating by the European Organization for Research and Treatment of Cancer (EORTC QLQ-C30). Conclusions show that Quality of Life is lower on patients on Home Enteral Nutrition when compared to those of general population, nutritional status influence the variance on Quality of Life up to 13% and that in competent patients self-rating was in line with proxy rating results. In the sub-group of patients with a 4 month follow-up, nutritional status was reported to stabilize or increase
slightly (regardless of patient consciousness and existence of malignancy), physical function improved and fatigue decreased.

A study conducted between 2000 and 2001 in the United Kingdom (Edington, 2004) aim to determine if nutritional supplementation in older patients after discharge from the hospital would improve nutritional status and functional outcomes, reducing healthcare costs. The *EuroQol 5D* questionnaire was used to assess Quality of Life and results after 24 weeks show no significant differences on nutritional status, Quality of Life, health status or health outcomes between groups, demonstrating that nutrition support in malnourished elderly patients should be done in a preventive way, as a part of routine care.

One element frequently discussed in home nutritional support is the expectation of families regarding the benefits of HAN implementation. A study in two North Carolina hospitals, in the United States, compared and assessed the expectations and outcomes of patient surrogate, when patients started to receive Enteral Nutrition through a Feeding Tube (Carey, 2006). In this prospective cohort study, comprising 288 patients with a mean age of 65 years and with primary diagnosis of stroke, head or neck cancer and neurodegenerative disorders, surrogates were interviewed after tube feeding insertion and after 3 and 6 months. In a scale from 0 to 10, the perceived global Quality of Life at baseline was low (4.6) and families anticipated that it could be improved up to 8.0 and this expectation did not change over time (3 and 6 months). The clinical outcomes did not match family high expectations, showing an over estimation of survival and functional recovery. As stated by the authors, providers and families need better communication and information about this nutritional support procedure.

In Japan, a study performed by a hospital (Shintani, 2013) followed retrospectively 80 patients with neurologic impairment (with associated swallowing dysfunction) receiving home nutritional care from the hospital team (consisting of a doctor, a visiting nurse, a home-helper, a rehabilitation specialist and a medical social worker). Survival period presented significant differences according to nutritional support: for self-feeding oral-intake group mean survival was 399 days, for Percutaneous Endoscopic Gastrostomy group mean survival was 736 days and for Home Parenteral
Nutrition group was 725 days. Despite achieved results, authors consider that no clear assumptions should be taken.

Cost and Benefits studies

Economic evaluations should present, for the alternatives under analysis, costs and consequences. Unfortunately, the great majority of studies found on this literature review for Home Artificial Nutrition, assess separately these outputs, making much more difficult to weight the costs and benefits of therapy implementation. In Table 1, an overview of key parameters for the selected economic studies evaluating costs and consequences, are listed; articles appear by chronological order, according to the year of publication.
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<th>Author/Year/Country</th>
<th>Study Type/Number of patients</th>
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| Detsky, 1986, Canada | Cost Utility Analysis - 73 patients (46 chronic and 27 acute), mean age of 42 years old | Home Parenteral Nutrition - No restriction (need HPN, only one with active malignancy) | Measure incremental health care costs and incremental health outcomes | **Costs:** included direct hospital costs and support departments, solution, physician services and various procedures and those received outside the specific hospital (Canadian dollars 81/82).  

**Outcomes:** Three techniques for assessing quality of life (utility) were used: category scaling and time trade-off as described by other authors and a new technique developed – “direct questioning of objectives”.  

For chronic patients the alternative considered was Hospital PN, for acute patients Hospital PN or no nutritional support.  

When compared with hospital Parenteral Nutrition alternative, over 12 years frame and for all patients, savings of 19,000 dollars were verified with 3.3 QALY’s gained. If considering only acute patients saving of 167,000 dollars were obtained with 2.2 QALY’s gained; if only chronic patients were considered an incremental cost of 16,800 dollars/QALY gained was obtained.  

If the alternative considered was no Parenteral nutrition support, incremental cost for the entire cohort was 27,000 dollars/QALY gained and for acute patients the value was 52,000 dollars/QALY gained. Productivity gains were not considered. |
| Richards, 1996, United Kingdom | Cost Utility Analysis - 64 patients, mean age of 44 years old | Home Parenteral Nutrition - Patients with intestinal failure (none patient with AIDS or active cancer) | Evaluation of HPN for intestinal failure determining its cost utility | **Costs:** includes those relevant for National Health Service, but not costs attributable to patients such as employment, travel costs and time.  

**Outcomes:** utility scores obtained from *EuroQol Health Status Questionnaire*. Quality Adjusted Life Years gained calculated by multiplying length of survival by the quality-of-life index, with a discount rate of 6% per year.  

Study made in the broad perspective of the National Health Service with a Sensitivity analysis performed.  

Total cost for 4 years of treatment is 142 089 pounds in Home Parenteral Nutrition and 312 595 pounds for an in-hospital patient (saving of 170 506 pounds). Mean utility score for HPN patients was 0.52 (0.61 for patients under 44 years and 0.28 for older patients).  

The cost per QALY in a HPN patient surviving 4 years (compared with the alternative of no treatment), was 69,000 pounds (for patients over 55 years 127.000 pounds and 58,000 pounds for patients under 44 years). If considering two episodes of line sepsis cost per QALY would rise to 71,000 pounds. Treating patient in hospital would increase the cost to 190 000 pounds per QALY.  

Home care is about 65 per cent more cost-effective than hospital care and the longer a patient survives on HPN the more cost-effective the treatment will become. |
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| Reddy, 1998, United States| Cost and outcome analysis.    | Home Parenteral Nutrition (23 patients), Home Enteral Nutrition (9 patients). 7 patients were on both nutrition therapies. - No restriction | Cost and clinical outcome analysis and health status assessment.                                                                                               | Costs: hospitalizations (including number of days), clinical visits, home nursing visits, laboratory testing, associated drug therapy, parenteral and enteral solutions, enteral tube feeding, pump rental and administration sets were included. Expenses calculated from a payer perspective and considered for 1996, with a discount rate of 5% applied to the years 1991 to 1995.  
Outcomes: Clinical outcomes were measured by hospitalization rates, complications and clinical/nursing visits per year. Questionnaires sent to determine the influence of therapy on lifestyle (32 have replied) and a general health status questionnaire, the Short Form 36-item survey (25 have replied).  
Average costs were $70,000 on HPN and $18,000 on HEN. Majority of expenses due to parenteral solutions or enteral tube feedings ($55,000 dollars and $10,000 dollars respectively, based on Medicare) but, hospitalization costs might exceeded those of nutritional support.  
The annual number of hospitalizations per patient on PN ranged from 0.52 to 1.10, compared with 0 to 0.50 in EN. HPN patients were usually hospitalized for 3 to 5 days per year due to therapy complications; HEN patients typically did not require hospitalization for complications of therapy. Typical HPEN patient suffer one/two complications per year.  
Obtained Quality of Life was significantly lower than the general population and similar to patients on dialysis and no significant differences between the SF-36 scores were found between HPN and HEN groups. Areas more affected were travel, sleep, exercise, leisure and social life. |                                                                                                                                                                                                                                      |
| Luis Roman, 2003, Spain   | Cost -Efficiency analysis     | Home Enteral Nutrition (oral route on 80% of patients) - No restriction (mostly cancer) | Evaluates direct costs and using biochemical and nutritional monitoring values as reference point for efficacy assessment. | Costs: only direct costs on formulas and equipment (nasoenteral, gastric or jejunum tubes) were included.  
Outcomes: several biochemical parameters and anthropometric parameters (triceps skin fold, arm circumference, weight, height and body mass index) were evaluated.  
A total cost per full treatment and per patient was 1,800 euros, with a daily average cost of 18 euros. Oral Nutritional Supplements costs were 5.5 euros per day, while daily expenses in Enteral Tube Feeding were 29.6 euros.  
A significant improvement of biochemical and anthropometric parameters in patients with Home Enteral Nutrition has been verified. Increase of 1 g/dl of albumin had an average cost of 624 euros and an increase of 1 kg of weight had an average cost of 5152 euros.  
Patients with greater expenditure were those with cancer. |                                                                                                                                                                                                                                      |
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<td>Arnaud-Battandier, 2004, France</td>
<td>Observational, prospective, longitudinal, cohort study with 12 months follow-up. - 378 patients</td>
<td>Oral Nutritional supplements - Patients with malnutrition, over 70 years, living in community.</td>
<td>Assess the cost of malnutrition and related comorbidities and determine the impact of ONS on outcomes.</td>
<td>Costs: medical care consumption (prescribed supplementation products, general practitioner, nursing, physiotherapist and specialist visits, examinations and hospital admissions).</td>
<td>Outcomes: nutritional status, malnutrition-related comorbidities.</td>
<td>Two groups of physicians were selected based on historic prescribing practice: one group with rare and another with frequent prescription of ONS. The perspective of economic evaluation was the Health Insurance System.</td>
<td>Medical care consumption including the cost of hospital care, nursing care and other medical care was lower in the group with frequent prescription of Oral Nutrition Supplement (723 euros saving per patient). Considering the cost of oral supplementation (528 euros), mean saving per patient over the 12 months follow-up was 195 euros in the group with frequent prescription of ONS. Nutritional status improved over time in both groups. Average length of stay in hospital was 1.3 days less in the group with frequent prescription of ONS and nurse visits for self-care, medication intake and decubitus ulcer care were also less frequent for the same group.</td>
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<td>Baxter, 2005, Brazil</td>
<td>Retrospective, paired and controlled study. - 56 patients (30 on Study Group and 26 on Control Group)</td>
<td>Parenteral and Enteral Nutrition / Surgical patients with digestive diseases.</td>
<td>Costs and benefits of nutrition therapy (comparison of integrated hospital-home model and exclusively hospital).</td>
<td>Costs: expenses of nutritional care, pharmacologic therapy, health care team and daily hospital costs (adjusted for 2001, according to the hospital inflation index).</td>
<td>Outcomes: Nutritional benefits were evaluated using the adapted index of nutritional rehabilitation. The same nutritional care was applied in both groups and the study was conducted from the patient perspective (nutritional benefits and length of hospitalization) and the institution (cost, optimization of hospital bed usage and resource optimization).</td>
<td>Both groups achieved the same nutritional benefits and the same rate of complications but expenses were 3 times lower for the hospital-home model group. Length of hospital stay was reduced 2.7 times, optimizing hospital bed usage. Cost-benefit ratio showed an important savings per patient for the institution (3100 United States dollars), arising namely from days of hospitalization avoided and prevention of surgical complications.</td>
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| Elia, 2008, UK      | Cost-Utility Analysis - Clinical data from 9895 patients (British Artificial Nutrition Survey database); 25 patients evaluate Quality of Life. | Home Enteral Nutrition (Tube Feeding) - Patients on Home Enteral Nutrition with cerebrovascular accident | Determine cost per quality adjusted life years for patients with cerebrovascular accident (home or nursing home). | Costs: Enteral Tube Feeding and ancillaries, delivery by a home care company, four days training in a hospital, blood tests (including labels and transport) were included. Prices considered for 2004/2005, without discounting.  
Outcomes: Mean quality of life score measured on the EuroQol visual analogue scale by questionnaires sent to a random sample of 25 patients. Clinical data collected from British Artificial Nutrition Survey on 9895 patients who started this home nutritional support between 1995 and 2005.  
A sensitive analysis was performed and included variation on survival, home visits, Quality of Life, payment of nursing homes, hospital treatment and annual discount rates. | Calculated Quality of Life on patients was estimated to be 0.47 compared with a mean score of 0.75 for a representative sample of the general UK population between 70 and 80 years.  
The following incremental costs were obtained (compared with the control group of no Enteral Tube Feeding): - 12.800 pounds/QALY for patients at home - 10.300 pounds/QALY at a nursing home (if no costs were supported by the state) - 68.100 pounds/QALY at a nursing home (if all costs were supported by the state) - 171.700 pounds/QALY for patients at treatment in National Health Service hospital.  
If the quality of life was only half of that observed for home patients, the cost/ QALY would double to 25.600 pounds. In addition to Quality of Life, mortality has also a significant impact on the results, unlike frequency of home visits by health professional. |
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| Freijer, 2012, Netherlands | Health economic model - Analysis based on 720 223 patients | Oral Nutritional Supplements - Population older than 65 years old in Netherlands | Evaluate the budget impact of ONS usage in patients over 65 years, for treatment of Disease Related Malnutrition in the community. | **Costs:** based on ONS costs and costs of illness of Disease Related Malnutrition.  
**Outcomes:** Re-hospitalization considered a clinical outcome and used as efficacy measure.  
The study was made in a limited societal perspective, comparing the use versus non-use of ONS. Clinical probabilities and resource utilization were based on clinical trials and published literature, considering a reduction of 27% on Disease Related Malnutrition. A sensitivity analysis has been performed and study time horizon was 12 months.  
Oral Nutritional Supplement use have reduce the costs from 275.000 to 262.000 million euros, leading to a cost saving of 13.000 million euros (4.7% savings), when treating 720 223 patients.  
Additional costs of ONS (57 million euros) are balanced by a reduction of the total costs of DRM due to a reduction of health care costs like re-hospitalization (70 million euros).  
The use of ONS in this group of patients may lead to a positive impact on the national health care budget in the Netherlands, confirmed in nearly all sensitivity analysis. | |
| Klek, 2014, Poland | Observational multicenter study - 456 patients | Home Enteral Nutrition / No restriction on the underlying disease | Compare clinical value and cost-effectiveness of Home Enteral Nutrition with commercial formulas and Nutrition Support Team. | **Costs:** hospitalization expenses, based on diagnosis-related group system adopted in 2007 by Polish NHS.  
**Outcomes:** comparison of number of complications, hospital admissions, length of hospital stay, intensive care unit stay, biochemical and anthropometric variables.  
A 12 month period was compared: first, patients were tube fed a homemade diet and not monitored; secondly, patients received enteral commercial formulas delivered by home nutrition company and monitored by a nutrition support team.  
HEN with commercial formulas and nutritional follow-up improves clinical outcomes and decreases health care costs.  
Mean annual costs of hospitalization were reduced to less than one third, from 6500 to 2070 US dollars.  
After Home Enteral Nutrition implementation a weight gain and a reduced incidence of infectious complications (37.4% compared with 14.9%), including the 2 most common - pneumonia and urinary tract infection - were verified.  
Additionally, a reduction on the number of hospital admissions (1.98 to 1.26) and length reduction of hospital stay (39.7 days compared with 11.9 days) was proved. | |
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<td>Naghibi, 2014, United Kingdom</td>
<td>Health economic evaluation and systematic review - 437 patients (in 12 studies)</td>
<td>Home Parenteral Nutrition / Patients with inoperable malignant bowel obstruction</td>
<td>Meta-analysis of survival, quality of life and cost-effectiveness of Home Parenteral Nutrition</td>
<td>Costs: per day considered: 150 pounds on HPN (considered for 7 days per week), 2014 pounds on hospital admission, 1580 pounds on chemotherapy as well as other costs (outpatient and home care visits). Outcomes: measurement of survival length, QoL (extracted and evaluated, mostly based on validated tools, where changes over time could be assessed) and any cost or cost-effectiveness outcome measures. On the basis of the above information a utility value of 0.5 (scale from 0 to 1) was used in the base-case analysis, both for the HPN and control groups Sensitivity analysis performed for survival length, utility, costs and resource use.</td>
<td>Studies used different tools to assess QOL and it was not possible to subject them to a meta-analysis; some use validated tools, others information provided solely and directly by the patients and others a mixture of information from patients, family members and clinician’s opinion. Mean survival of 116 days, with 45% and 24% still alive at 3 and 6 months, and only 2% survival at 12 months (base-case survival time in the control group was assumed to be 14 days). The Incremental Cost-Efficiency Rate for the palliative malignancy HPN patient group, at base-case cost and utility, was 177.000 pounds per QALY. In sensitivity analyses, the ICER in all cases remained above 123.000 pounds per QALY gained and changes in the utility assumption for the treatment group would lead to the most substantial effect on ICER, followed by costs of parenteral nutrition and survival length. Meta-analyses reveal a short survival and health economic analysis demonstrates high associated costs and, from a purely economic approach, it would need strong justification for therapy implementation.</td>
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About the studies publication year it can be noted that Home Artificial Nutrition is a clinical therapy being implemented, at least in some countries, for a few decades but the number of studies has not registered a strong increase across the years. The economic crisis and financial restraints, being felt across the world in recent years, might be an opportunity to increase awareness about the need to establish solid evidence for cost-effectiveness of nutritional support therapies. All studies compare the costs and outcomes of a given nutritional support therapy.

Evaluating the type of presented studies, three of them are Cost Utility analysis presenting the results on costs per QALY gain, as recommended by several governments and institutions, enabling to measure the impact of the therapy on patient Quality of Life. Two studies are considered Cost-Effectiveness since outcomes are presented in natural units, and in other three, outcomes are presented in natural units (like complications and hospitalizations avoided), converted into monetary costs. The remaining two studies were an economic model development to assess the budget impact of Oral Nutritional Supplements in elderly (Freijer, 2012) and a meta-analysis review of articles about patients with inoperable bowel obstruction that undergo Home Parenteral Nutrition (Naghibi, 2014). The number of patients enrolled in the studies varies from a few dozens to a few hundreds, with a lower number of patients being registered in Home Parenteral Nutrition studies. Two of the publications mentioned thousands of patients, but they were only considered for clinical data collection in one case, and economic model development in other case. All of the studies refer to a specific country and some of them refer to a specific region or hospital center. The great majority of studies is observational, both retrospective and prospective, due to ethical issues mentioned by several authors of carrying a clinical trial recruiting patients deprived from nutritional support (Klek, 2014).

Five studies have been done for Home Enteral Nutrition (two of them for Oral Nutritional Supplements), three for Home Parenteral Nutrition, and two for both HEN and HPN. As for underlying disease and clinical condition, three of the publications made no restrictions about it, ONS studies were performed in older patients, one HEN study was done for patients after cerebrovascular accident and HPN articles were performed for
intestinal failure and other for bowel obstruction. Most of the clinical situations presented are in line with the typical epidemiology verified on each nutritional support.

Costs considered were generally direct ones, arising from hospitalization costs including support departments, nutritional care (parenteral and enteral solutions) and associated equipment such as tube feeding, pumps and infusion sets, healthcare professional services, examinations and other clinical procedures, laboratory tests, pharmacologic therapy, home visits, nursing visits, home care delivery and training. The outcomes referred in the studies were patient Quality of Life, malnutrition-related comorbidities, survival length, hospital admission, number of complications verified or avoided, hospital stay length, intensive care use, nutritional benefits, biochemical and anthropometric values (weight, height, body mass index), clinical and nursing visits per year. This wide variety of items considered for costs and consequences makes very difficult to compare them and establish firm conclusions as showed by the above mentioned study consisting of a systematic review (Naghibi, 2014), where, for a specific nutritional support and underlying disease, the author was not able to perform a meta-analysis on Quality of Life, due to the different tools use to assess it.

Some studies do not specify the time horizon used, but the others range from periods of 12 months up to 12 years. Taking in consideration that the study time horizon should accompany therapy duration and its consequences, it would be advisable that studies could have a time horizon of few years, with some exceptions, like when referring to patients on a palliative stage of the disease. The majority of studies were performed from the National Health Service perspective with the costs calculated from the payer perspective.

Globally, Quality of Life in Home Artificial Nutrition was found to be lower than general population affecting several domains of daily life, and according to one study similar to patients under dialysis (Reddy, 1998). No difference in nutritional benefits and complications rates were found between hospital support and home support, proving that this home therapy is effective and safe. Costs, number of hospitalizations and length of hospital stay were higher on patients on HPN when compared with those on HEN.
HEN studies show a reduction on incidence of infections complications, reduction of hospital admission and length of stay, improvement of biochemical and anthropometric parameters (like weight), leading to a decrease of hospitalization costs. Both studies focusing on Oral Nutritional Supplements show a reduction of re-hospitalizations and medical consumption (superior to ONS cost), showing that this nutritional support in elderly living in the community may contribute to healthcare cost saving.

The study focusing on HPN implementation in Canada (Detsky, 1986) concluded that when compared to hospital Parenteral Nutrition, HPN would result in a net saving cost and increase in QALY; when compared with no nutritional support, the baseline for the entire cohort would be 27,000 dollars per QALY gained. Other Cost-Utility study on HPN implementation (Richards, 1996) show a mean cost per QALY of approximately 69,000 pounds that would increase to patients over 55 years old and decrease to those under 44 years, due to the difference verified in the utility. HPN showed to be about 65 per cent more cost-effective when compared to hospital Parenteral Nutrition and with better results for younger patients.

Results for the study consisting in a systematic review (Naghibi, 2014) show an ICER of 177,000 pounds per QALY in patients with inoperable malignant bowel obstruction, revealing a short survival with associated high costs for HPN. Healthcare professionals should accurately identify those patients likely to survive for long enough to benefit from this treatment.

In the HEN study focusing on patients with cerebrovascular accident (Elia, 2008), results show 12,800 pounds per QALY gained at home, 68,100 pounds per QALY gained at nursing home when costs are supported by state and 171,700 pounds per QALY gained at NHS hospital. The treatment compares favorably with other forms of intervention when the state does not contribute significantly for expenses since, for the study private cost were not included.

Patients subject to Home Artificial Nutrition revealed poorer Quality of Life scores when compared with general population but higher scores can be obtained, in
younger patients, without active cancer and with more than caregiver. Oppositely, changes in food ingestion and family dependence can deteriorate Quality of Life. Results for Quality of Life in HEN patients can be compared with those obtained on patients with chronic obstructive pulmonary disease and for HPN with those patients undergoing dialysis. Therapy implementation is generally more cost effective in pediatric population due to higher life expectancy. This is in line with studies demonstrating that the longer a patient survives on Home Parenteral Nutrition the more cost-effective the treatment becomes; this topic is of particular importance when evaluating the nutritional therapy implementation in patients in a palliative stage of the disease.

Costs are usually calculated from the perspective of hospital or insurer, without assessment of a wider social and economic impact. Parameters such as household of a child receiving HPN, income losses of caregivers, emotional costs and the broader impact on the family are rarely calculated. HPN is an expensive therapy but the lack of alternatives in most of the situations, justifies a careful decision for nutritional support implementation.

Most of the studies are made from the National Health Service perspective, with a relatively short time horizon and made for a specific country, region or even hospital center. Clinical trials are not frequently performed due to ethical reasons, but observational studies might raise some bias and misevaluations. The generality on studies underline the importance of a Nutritional Support Team for successful implementation of HAN programs.
CHAPTER VII - Future of Home Artificial Nutrition

Several crucial challenges are already being posed in the present and many more will arise in the future, for economic evaluations of Home Artificial Nutrition programs. Economic evaluations are increasingly becoming an instrument for decision makers to maximize societal benefits in contexts of scarce resources but, when referring to healthcare, clinical variability among patients may present some obstacles and ethical issues might be raised.

First, it is important to determine the patient nutritional risk at all healthcare settings, in adequate way, and with the help of suitable and accurate tools (BAPEN, 2008). Early diagnosis and treatment of malnutrition in the community will improve the outcomes, lowering costs, and nutritional monitoring should be performed throughout the entire treatment.

Patients undergoing Home Artificial Nutrition deal with severe physical, physiological and social challenges from the nutritional support (including complications, technology and medical dependences), in addition to those presented by the underlying disease. Health care professionals working in the home care setting should be aware of these challenges and help patients and their families to overcome difficulties.

For determining the impact on Quality of Life of Home Artificial Nutrition interventions, several instruments, scales and domains are being used. Some use general questionnaires, others adopt specific disease questionnaires and for other studies, specific questionnaires have been developed. It would be beneficial to create specific instruments for assessing Quality of Life, developed specially for Home Parenteral Nutrition and Home Enteral Nutrition, allowing a more accurate measurement of variations over time and permitting outcome comparison among studies.

One of the most important parameters for successful implementation of home nutritional support is the relation between healthcare professionals, patients, and their respective families. According to NICE recommendations, health care professionals should ensure monitoring and follow-up, reviewing indications, routes, risks, benefits and goals
of nutritional therapy when needed. For these tasks, professionals supporting patients at home should have enough experience and expertise, to match both patient and family expectations as well as demanding technical requirements. Patients and their family must consider the positive aspects of being in the home setting with the challenges and difficulties of administering complex therapies at home.

For successful therapy implementation, patients and their families (or caregivers) should receive information, training and educational interventions from the multidisciplinary team, learning how to manage procedures of nutritional delivery and instructions of how to solve common problems or complications. A structured program of education, set for Home Artificial Nutrition, provides to patient and families a higher sensation of trust and security, with beneficial effects on therapy outcome, either by keeping the nutritional state and improving quality of life. Protocols should be elaborated for use in different health care services (hospitals centers, primary care) to achieve treatment harmonization and family information, promoting patient self-care and independence, whenever clinical conditions allow it. Information should be presented in sources, formats and languages appropriate to individual characteristic such as gender, physical needs, culture and stage of life. A routine and emergency contact should be available to communicate with an healthcare professional, and contact details should be available for reaching the homecare company provider, in case of equipment trouble.

A complementary support with growing importance is being given by voluntary or non-governmental support groups, for patients receiving artificial nutrition. One example is The Oley Fundation that provides educational resources, social support and outreach services. It also helps in lifestyle adaptation promoting experience sharing between patients, families and caregivers. This kind of interventions might have a positive impact on patient and caregiver Quality of Life (Chopy, 2014) by reducing, for example, depression, fatigue and isolation symptoms. It has about 12.500 members, including clinicians and families, who handle with Home Parenteral or Enteral Nutrition. Also in the United States, other organizations have been created with the purpose of helping families that take care of their patients. The National Alliance for Caregiving is a nonprofit coalition of national organizations focusing on issues of family caregiving that includes
professional associations, service organizations, disease-specific organizations, governmental agencies and corporations. The National Family Caregivers Association supports, empower, educate and promote Quality of Life of families taking care of relatives with chronic illness, aged or disabled; the Family Caregiver Alliance promotes programs and initiatives to support and sustain families nationwide caring for loved ones (Winkler, 2006).

BAPEN (British Association of Parenteral and Enteral Nutrition) is a charitable association founded in 1992 in the United Kingdom that brought together different healthcare professionals such as dietitians, doctors, nurses, patients and pharmacists, dedicated to improving nutritional care. In 1996, BAPEN has created the British Artificial Nutrition Survey (BANS) in order to audit and research nutritional care, monitor artificial nutrition in hospitals and in the community, evaluate treatment outcomes, establish structures of services of artificial nutritional services, assess care standards and identify problems associated with use or lack of artificial nutrition. Also in the United Kingdom, a patient association has been set up, Patients on Intravenous and Nasogastric Nutrition Therapy (PINNT), producing surveys relevant for Home Artificial Nutrition management, helping patients to solve their problems and complains, influencing public opinion and government decisions.

One of the key points for the development of Home Artificial Nutrition programs is the existence of legislation and regulations that promote harmonization of clinical practices and assure equal access between patients. Legislation in this area should present a balance between the payer perspective, that needs to ensure a rational resource distribution and limiting overuse situations, and professionals (together with families) who try to ensure to patient the best available resources to improve nutritional status, Quality of Life and improve underlying disease prognosis. In Europe, some countries have no specific legislation (despite supporting these home nutrition programs), while others have national or even regional legislation, leading to a differential treatment among patients with the same clinical conditions. The issuing of legislation for Home Artificial Nutrition reveals political awareness for the malnutrition issue on the community setting and allows, at the same time, the creation of tools for the
acknowledgment of prevalence in the community and sharing of clinical practices and program implementation.

The creation of national registrations for Artificial Nutrition has been developed in several countries with the objective of gathering information about these clinical practices. Data collection about the use of nutritional support in the countries, allow decision makers to take informed and rational choices.

In Spain, NADYA - working group of SENPE (Sociedad Española de Nutrición Parenteral y Enteral – Spanish Society of Parenteral and Enteral Nutrition), publishes since 1992 an annual report on patients undergoing home nutritional support. It quantifies the use of Home Artificial Nutrition in Spanish territory, characterizing pathology and age distribution, administration routes, among others.

Another registry created in Spain in 2003 focus on pediatric Home Enteral Nutrition practices, the NEPAD (Nutrición Enteral Pediátrica Ambulatoria y Domiciliaria - Pediatric Ambulatory and Home Enteral Nutrition).

The American Society for Parenteral and Enteral Nutrition (ASPEN) has developed a web-based registry called Sustain, in early 2011, to collect information about patients and populations who require Home Parenteral Nutrition in the United States. The registry is open to all sites (hospital and home based) providing care to Home Parenteral Nutrition patients, promoting institutional benchmarking. It measures outcomes associated with this therapy, publishing findings to improve the quality of care in these patients and obtained data can be used to help public policy decisions (Guenter, 2012). This new tool replaces the previous registry, responsible for data collection of nutrition support programs, cancelled on the nineties due to cost maintenance.

Home nutrition organizations are increasing their service portfolio to other areas such as day care, medical and therapy services, personal care and management of specific diseases. The pharmaceutical industry has also become interested in developing Home Artificial Nutrition programs (Enteral or Parenteral) and is changing the concept of medical nutrition delivery to a more coordinated, flexible and complete home care service, meeting expectations from both patients and health care professionals by
offering a comprehensive range of services. Home care companies must define procedures and policies consistent with existing regulation, and standards of care should be subject to independent audits and customer satisfaction surveys, as already occurring in the United States. Process certification (issued by payers, for example Medicare) of home care agencies, require adherence to federal requirements for patient care and management, may initially present an investment from a technical level, but might increase business opportunities.

The evolution of nutrition support consumables by manufacturers (nutritional infusion bags, enteral preparations and oral supplementation in different presentations), led to the availability of preparations increasingly adapted to patients nutritional requirements, with positive impact on health results. One of the examples is the use of industrially prepared enteral formulas that, compared with home-made formulas corresponding to the blend of conventional food, have a more complete nutritional composition, lower rate of catheter obstruction and less microbiological contamination.

Scientific Societies should help determining the safety and effectiveness of this kind of home care programs, by issuing standard protocols and clinical guidelines. Only a homogeneous clinical guidance would allow careful patient selection and a correct treatment implementation, adapted to each case. The existence of a multidisciplinary Nutritional Support Team (NST) in this home support therapy is essential. This team should be composed by different health care professionals (like physicians, dietitians, pharmacists and nurses), monitoring patient’s progress and making recommendations and changes accordingly. The determination of a patient nutritional status and the correct choice of nutrients matching patient needs are essential for maximizing the outcomes of Home Artificial Nutrition. The Nutrition support team should be coordinated with the primary care setting and team members should have experience of care provision in the community, namely when referring to Home Enteral Nutrition. It is very important that this team can provide a flexible service that can fit patient lifestyle, like scheduled restrictions.
A new challenge has emerged in the latest years, namely in Home Enteral Nutrition: therapy overuse. Some studies point out the irrational use of tube feeding in some patients group where positive outcomes have not been clearly shown, where the idea of “doing something” superposed the expected treatment efficacy. To avoid these situations, authors recommend tighter reimbursement and payment associated to performance measurement.

More research would be necessary to better understand the cost-effectiveness of home nutritional support and the importance of this intervention to healthcare systems. All the involved stakeholders (organizations, home care companies, insurance companies, regulators and governments, payers) should work together for gathering data that can assess thoroughly the value and outcomes of this home support.

In Portugal, much work is to be done in Home Artificial Nutrition, starting by the creation of a legislative framework and a national registry database that can help in establishing the national epidemiological reality. Clinical protocols should be elaborated to harmonize access and implementation of this home care therapy, tasks that nowadays, rely on each hospital center. Nutritional support teams should be present in the hospital setting and primary care and perceived as a major contribute for quality of care and patient outcomes. Better coordination and flow of information is needed among the diverse health settings, for example between hospital centers and primary care, assuring integrated care, allowing patients to have a solid follow-up with harmonized care and established nutritional goals.
CHAPTER VIII – Conclusions

The problem of malnutrition in the community setting still is not sufficiently recognized by healthcare professionals, scientific researchers and political decision makers. Malnutrition is a multifactorial condition, with a wide range of causes (from pathological to pharmacological, social and environmental). It is considered a risk factor in health outcomes, delaying clinical rehabilitation and increasing the number and severity of complications associated with infections and primary diseases. This increases healthcare expenses and some national studies have demonstrated that the economic impact in health care budgets can reach values with significant financial impact.

Home care development has been driven resource allocation from hospital to the community setting. For this development, a few factors have contributed decisively: patient empowerment (patients are more informed about the options and condition), technological development, expansion of new community based services and early discharges from hospital setting due to financial restraints.

Home Artificial Nutrition is considered as a relatively safe therapy which can be provided by the hospital center, community based provision or commercial home care service.

Home care agencies provide, nowadays, a comprehensive range of services after patient discharges like equipment supply, patient information and support, day care, medical and therapy services, personal care, among other, in order to meet expectations from both patients (and their families) and comply with healthcare providers requirements. The importance of providing a coordinated, flexible and complete home care service should be highlighted.

Home Parenteral Nutrition is a very complex therapy, involving the correct handling of several techniques and presenting higher risk of complications, with serious consequences. HPN programs have a steady increase in the last decades and prevalence is higher in the United Stated when compared with European countries. The main two causes for this nutritional support are active cancer and gastro-intestinal diseases, mean
age of patients undergoing HPN ranges between 40 and 60 years old, and the mean treatment duration might range from a few months up to a few years.

Home Enteral Nutrition comprises Oral Nutrition Supplements and Enteral Nutrition through a tube feeding (Enteral Tube Feeding) that should be preferred when compared to Parenteral Nutrition. It seems to be more frequent in the United States, despite differences in Home Enteral Nutrition product classification and prevalence calculation. Neurological impairment and oncologic diseases are responsible for the majority of cases and, unlike HPN, the most common age groups for patients on HEN are the children and the elderly, with mean age for adults on this nutritional support, above 70 years old. Mean treatment duration range from a few months to over 12 months.

Legislative framework is a key point to establish the basis for nutrition support implementation in countries and should take into account payers and service provider inputs and, more important, patient well-being.

In Europe, Home Artificial Nutrition has been developed based on several national regulations and, in some cases nutritional support programs precede the existence of any type of regulation. Funding for Home Artificial Nutrition is relatively uniform in Europe, with public health services supporting the costs of Home Parenteral Nutrition, and bearing totally or partially the costs of Home Enteral Nutrition. Among European countries diverse implementation, reimbursement and access have been reported, with the private sector starting to have an increasing role in providing home care service. A positive association has been found between the number of years since the first regulation and the current HAN prevalence.

In the United States, HAN financing relies mostly on private insurance companies and governmental programs (such as Medicare or Medicaid). Development occurred when hospitals and insurance companies started to realize the financial benefits of early patient discharge to the home setting, leading to an increase of home care providers companies. Patient coverage changes according to the type of insurance subscribed and, while some have specific criteria for eligibility, many follow general Medicare guidance. Specific conditions must be met for therapy coverage like categorization of primary
diagnosis, mean therapy duration and ensuring that the implemented nutritional support is reasonable and necessary to maintain (or increase) patient health status. For both HEN and HPN, Medicare pays around 80% of total costs with the remaining 20% to be supported by the patient itself or other secondary insurance, if available. Home care companies are requested to have a significant knowledge in reimbursement mechanisms, ensuring an adequate delivery system and a skilled clinical management.

In Portugal, Home Artificial Nutrition is not legislated and no national registry for Home Enteral Nutrition and Home Parenteral is available. The existence of a Nutritional Support team is present in only one third of hospitals and only a small percentage have reported the existence of a Home Artificial Nutrition Support Unit. The Portuguese reality in HAN implementation is very diverse and two examples were presented: one hospital center provided materials for artificial nutrition but did not ensure a true home nutrition scheme while other, presenting a partnership with a pharmaceutical company, has a home care program including weekly visits, a permanent phone contact, periodic training, and home delivery of enteral formulas and other support materials. Since hospitals centers are normally responsible for HAN implementation, the lack of harmonization is leading to a differentiated access of the population to HAN programs.

Governments should decide about the distribution of limited financial resources for medical treatments, namely in those countries where health care delivery is based on social welfare systems and, for this matter, economic evaluations are becoming widely spread and are recognized as a key factor in the decision making process, both for medicines and other health care technologies.

Despite proven efficacy in different health care settings, some concerns have been raised about the lack of health related economic data for medical nutrition, even if, levels of prescription and reimbursement policies are currently assured by health care systems, public or private. Unlike for other health care technologies, such as medicinal products, health economics has not been required for coverage of medical nutrition interventions, neither reimbursement. In addition, nutritional therapy interventions are usually integrated in other healthcare processes, making very difficult to isolate and
evaluate the nutritional effect. As a consequence, some authors argue that medical nutrition should have a separate group in general health care reimbursement system, so that value for money can be assessed in these interventions.

Quality of Life is, *per se*, very difficult to calculate in any healthcare program since it describes a patient’s subjective experience, relying on emotional characteristics. Home Artificial Nutrition programs are recognized has having impact on Quality of Life of patients and their families due to its influence on daily routine, work environment, financial well-being and independence. Generic tools for measuring Quality of Life are not optimal but the use of specific instruments for chronic diseases might also present some challenges and lack of specific tools to measure and follow-up the efficacy of nutritional support has been identified.

Quality of Life should be assessed by the patient itself, if possible, but caregiver or healthcare professional rating is also possible and important, because it has been reported that even patients on permanent vegetative state experience Quality of Life changes. Some authors consider the additional need to identify and evaluate QoL on caregivers, due to the impact of home therapies in the familiar setting.

Globally, better results are obtained on patients with chronic conditions (such as Crohn's disease or motility disorders) when compared with oncologic patients, in younger patients (despite age itself should not be an eliminating factor), in patients with good self-esteem and good family support and in patients with more than one caregiver. Analysis show that the longer the patient stays on nutritional support, the more cost-effective the treatment will become (pediatric nutritional support are considered to be more cost-effective than adult nutritional support).

Cancer is one of the most frequent underlying diseases leading to support therapy and nutritional status is affected by this complex pathology in several ways: introduction of a pharmacological treatment, metabolic changes, lower food intake and increasing waste. Home Artificial Nutrition in patients with late stage cancer is controversial, since the major determinant for the outcomes is the oncological disease rather than the nutritional status, but studies point toward increased tolerance to
treatment, decreased rate of complications and optimization of balance between energy expenditure and food intake provided by this support. It is considered beneficial to implement nutritional support when death by starvation would precede death from the underlying disease and life expectancy is likely to be over 2 months.

Cost results obtained in the literature review differ significantly between them for a few reasons: type of nutritional support under evaluation, different country reality, publication year and types of costs considered. Home Artificial Nutrition programs may represent a cost reduction of between 60 and 70%, when compared with hospital inpatients, with a great share of saving arising from the avoided hospital costs; in Home Parenteral Nutrition, cost reduction might ranges from 25% to 60%. Home Artificial Nutrition programs seem to be more expensive in the United States than in Europe and the costs of Home Enteral Nutrition are estimated to be around 10% of those of Home Parenteral Nutrition. One situation frequently discussed, is when reimbursement systems (either assured by public or private payers) do not cover all expenses that arise from nutritional support. Financial constrains due to out-of-pocket expenses and non-reimbursed payments, associated with wage losses (due to decrease employment), decrease in insurance coverage and inability to pay monthly bills is associated with feelings of depression, affecting patient Quality of Life.

Home Artificial Nutrition studies present a variety of items considered as outcomes, some of them associated with nutrition status, for instance weight maintenance, biochemical and anthropometric parameters. Benefits of nutritional therapy program implementation are difficult to assess and two factors have a significant impact on these outcomes: patient underlying disease and age. Quality of Life in patients undergoing nutritional therapy depends from a variety of factors, such as: clinical history, clinical effects, social effects, economic effects and the handling of complex medical devices needed for Home Artificial Nutrition programs.

Patient and family expectation on outcomes should be adequate and reasonable, highlighting the need for better communication and information about this nutritional support procedure.
The great majority of studies found in this literature review for Home Artificial Nutrition, assess separately costs and benefits, making much more difficult to weight cost-effectiveness of therapy implementation; for those assessing costs and consequences simultaneously, a more accurate analysis has been performed.

Article publication data show that this therapy has been implemented for a few decades, however, the number of studies has not registered a strong increase across all these years. Economic crisis might be an opportunity to increase awareness about the need to establish solid evidence for cost-effectiveness of some nutritional support therapies. The majority of studies were Cost-Effectiveness studies, with outcomes being presented in natural units; in some cases, these results were also converted into monetary values. Only three of them are Cost Utility analysis and another was a meta-analysis review, also presenting results in cost per QALY gained.

The number of patients enrolled in the studies varies from a few dozens to a few hundreds, with a lower number detected in Home Parenteral Nutrition studies. None of the published studies collected data from more than one country and some of them refer only to a specific region or hospital center. The great majority of studies were observational, either retrospective or prospective, and the associated underlying diseases are according to the typical epidemiology of each nutritional support.

Costs considered in the studies were mostly medical direct ones with an underestimation of those attributable to the patient/family, while outcomes were very diverse, varying between Quality of Life, survival length, hospital admission and length of stay, number of complications, nutritional benefits, biochemical and anthropometric values, among others.

Some studies do not specify the time horizon used, but the others range from periods of 12 months up to 12 years. Taking in consideration that study time horizon should accompany therapy duration and its consequences, some timeframes could be insufficient for a complete and rigorous long term evaluation. The majority of studies were performed from the National Health Service perspective with the costs calculated from payer standpoint, lacking assessment of a wider social and economic point of view.
Quality of Life in Home Artificial Nutrition patients was found to be lower than in general population, affecting several domains of daily life, and no difference in nutritional benefits and complications rates were found between hospital support and home support, proving that this home therapy is effective and safe. Patients on HPN show higher costs, increased number of hospitalizations and length of hospital when compared with patients on HEN.

Almost all studies underline the importance of a Nutritional Support Team for successful implementation of HAN programs that, among other benefits, significantly reduce metabolic and mechanical complications; better outcomes have been reported in teams with more experienced health care professionals.

There is a general recognition about the need of further economically relevant research in medical nutrition field, due to the existence of few randomized controlled studies comparing hospital in-patients and home care patients. More studies on Quality of Life would be needed, with larger sample sizes, comparison groups and a wider range of diagnosis. Clinical trials are not frequent in this domain, due to ethical reasons of carrying a clinical trial recruiting patients deprived from nutritional support, but observational studies might raise some bias and misevaluations.

A global evaluation should be made to determine the cost-effectiveness of this home nutritional support therapy with contribution from all the stakeholders, from governments and payers, to groups of patients and home care providers. Home care models are believed to become more cost-effective in the future and over time, but it has been difficult to introduce home nutritional support issues in the political agenda, namely in some countries.

The purpose of this thesis was to get a better understanding of Home Artificial Nutrition health economics, assessing the current evidence for costs and consequences. We can conclude that this nutritional support therapy can be considered as cost-effective due to reduction of hospital costs, disease associated malnutrition and increase of patient’s Quality of Life. Costs associated with Home Parenteral Nutrition are high but, in
most of the clinical conditions, there are no viable alternatives and for Home Enteral Nutrition, patient selection is a key factor for increasing therapy cost-effectiveness.

There is no *gold standard* allowing uniform measurements and full comparison between studies. They present barriers for evaluation associated to data collection (patient age, type of underlying disease and therapy duration) and logistic factors. Further studies will be needed to assess how therapies should be implemented in a cost-effective manner, applying health scarce resources in a wise and appropriately way, maximizing the population well-being.
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Annex I – Results for systematic bibliographic search
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