Clinical Nutrition Research Through the Years


Claire James, RD, Head of Nutrition and Regulatory Affairs, AYMES International Ltd & **Emily Wong** MSc RNutr, Medical Reimbursement Manager, Nutricia, on behalf of BSNA

Despite Hippocrates acknowledging the connection between nutrition and health in his famous quote, *'let food be thy medicine and medicine by thy food'*, research into the role of nutrition as treatment only really started growing from the mid-20th century. This growing body of research underpins current dietetic practice and formed the foundation of the medical nutrition industry. Investing in future research is vital to truly unlock the power of nutrition as treatment and ensure innovation is kept at the heart of the medical nutrition industry. Together we explore the history of clinical nutrition research, key milestones and discoveries, and brave new frontiers looking to the future.

Laying the foundations

In the 20th century, some key nutritional science discoveries were made that paved the way for the beginnings of clinical nutrition. The early part of the 20th century was an era of vitamin discoveries, with thiamin being the first in 1926.[1] In 1932, vitamin C was isolated and definitively documented for the first time to protect against scurvy. By the mid-20th century, all the major vitamins had been isolated and synthesised. Their identification and use in studies led to the adoption of dietary strategies to tackle overt vitamin deficiencies, such as beriberi (vitamin B1), scurvy (vitamin C), rickets (vitamin D) and other deficiency conditions. However, the chemical synthesis of vitamins also allowed for vitamin supplementation to be an effective treatment strategy for deficiency conditions which is still widely used in clinical nutrition today.

The identification of single nutrient deficiencies and synthesis of vitamins also led to national food fortification practices to eliminate common deficiencies, such as mandatory fortification of margarine with vitamins A and D in 1942.[2]

Alongside the identification of vitamins, essential amino acids were also discovered through both animal and human studies in the late 1930s, paving the way for further research into the role of amino acids in the human diet.

A further key milestone in the UK was the publication of *The Composition of Foods* by Dr Elsie Widdowson and Professor Robert McCance in 1940.[3] This publication is still regarded as the foremost nutrition publication and the basis of most nutritional databases around the world. Shortly after this, the Recommended Dietary Allowance (RDA) was introduced in 1941 to guide planning of adequate nutrition for civilians.[4] The RDA was defined as: 'an average amount of the nutrient, which should be provided per head of a group of people if the needs of practically all members of the group are to be met'.

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These key developments, from the identification and synthesis of vitamins to the development of RDAs, lay the foundations for the application of nutritional science to the treatment of disease, developing into what we now know as clinical nutrition.

Clinical nutrition underpinning dietetic practice

It's easy to see the rise in clinical nutrition research, as a simple PubMed search using the term 'clinical nutrition' shows an exponential rise in publications beginning in the 1980s. See **Figure 1**.

In this time, our understanding of nutrition and its role in clinical medicine has grown significantly. From early research into basal metabolism and energy balance in disease states, to the growing research on nitrogen balance, protein and recovery, continued developments in clinical nutrition help improve dietetic support in disease and improve patient outcomes.

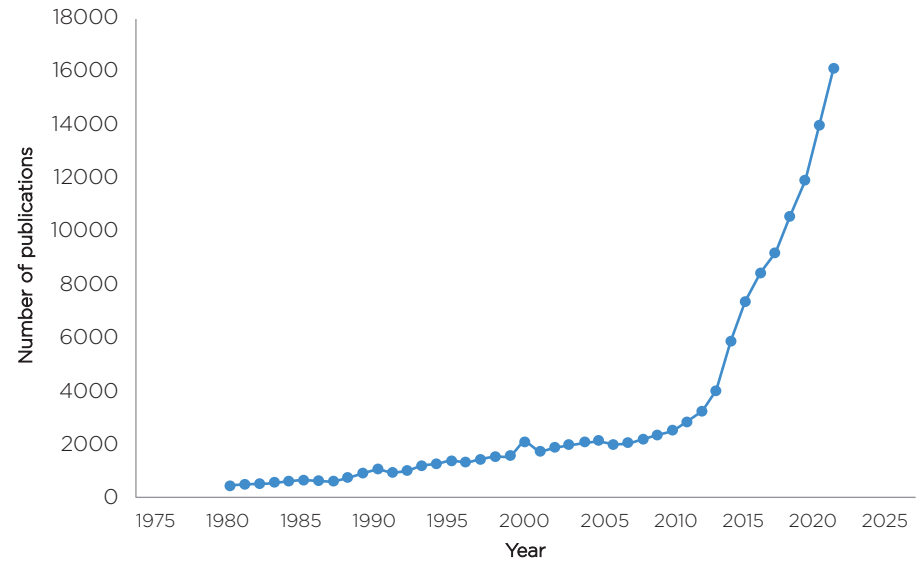
Much of the early research from late 20th century on nutrition support in critical illness was focused on energy intake and balance, and only in the 21st century did the attention of clinical research shift to the importance of protein intakes in illness.[5] Since this discovery, the focus on protein in maintenance and recovery continues, with studies working to determine the optimal protein intake in numerous conditions. Based on the analysis of extensive studies, NICE (CG32) in the UK recommend intakes of 0.8-1.5 g protein/kg/day in adults requiring nutritional support.[6]

With an ageing population, research on protein turned towards the maintenance of a healthy elderly population. Disease-related malnutrition and frailty are common issues among the aging, and research has highlighted the importance of nutrition in maintaining health, lean body mass and functionality alongside physical exercise. Protein requirements in the older population are higher due to age-related changes in metabolism, and especially in illness due to inflammatory and catabolic responses.[7] Based on a review of the global evidence and expert consensus, ESPEN guidelines recommend increased protein intake (minimum 1.0 g/kg/d) in older persons depending on their nutritional status, physical activity level, disease status and tolerance.[8]

As clinical nutrition research developed, so did the necessity to develop enteral formulations to administer nutrients in appropriate amounts to patients, leading to the formation of the medical nutrition industry. Much progress has been made from the early days of hospitals brewing their own enteral formulations (feeds made up of milk, eggs, meat broth, flour, etc.), as we now have convenient, ready-to-feed, sterile formulations delivering specific levels of nutrients available. As the importance of protein intake was investigated, the medical nutrition industry concurrently reviewed their product formulations to reflect emerging research.

Technological advances have also allowed the development of high protein feeds in lower volumes for use in critical illness or conditions with fluid restriction.

Figure 1: Rise in publications 1980-2021 based on Pub Med search term 'Clinical Nutrition'



(adapted from Pub Med timeline, search using the term 'Clinical Nutrition' – February 2022)

Not only is the quantity of protein key, but also the quality of protein. Research into the composition of different protein sources, their levels of essential amino acids and their metabolism led to optimal sources of protein being used in enteral feeds to deliver complete proteins. Other improvements in technical capabilities to produce energy dense, or compact, oral nutritional supplements have been shown to improve patient compliance to prescribed volumes.[9]

As the nutritional care of patients moved from the acute setting to the community, a need to make nutrition support available on prescription was recognised. The Advisory Committee on Borderline Substances (ACBS) was formed to assess enteral nutrition formulations and their suitability to be prescribed at the NHS' expense for specific patient groups in the community. Established in 1971, the ACBS remains the body that assesses and approves applications for borderline substances to be made available on prescription in the community today. Alongside community prescription, homecare services were developed by the medical nutrition industry to deliver nutritional products and any associated ancillaries directly to patients' homes, with supporting nursing care.

Standardised medical nutrition products have also allowed for further advances in research. With enteral feeds delivering specific nutrients, studying the impact of standardised formulations on clinical outcomes became easier for researchers. Research has shown that the use of oral nutrition support in the community can improve clinical outcomes, quality of life, and reduce number of hospital re-admissions, length of stay, ultimately improving patient recovery and reducing spend in the acute setting.[10-13]

New frontiers of clinical research

As we discover more about clinical nutrition, we also uncover more questions. There are constant developments in clinical nutrition, from the isolation of nutrients previously undiscovered to clinical nutrition in new disease areas, such as COVID-19 in its acute treatment and management of Long COVID.

Exciting research into the gut microbiota from the ill to the healthy, from infants to elderly, could also influence clinical nutrition as we know it today. In recent years, infant feeds containing pre- and probiotics have been introduced to clinical practice, and the long-term impact of this is only just starting to be studied.

With increasing prevalence of cancer and improvements in treatment and survival rates, much research is focused on the management of these diseases. Nutrition impacts clinical outcomes throughout the cancer treatment process, from baseline nutritional status, during/post treatment or pre-/post-operatively, to the maintenance of nutritional status during recovery, especially in the management of cancer-related malnutrition and cachexia which are commonly seen.

As the breadth and depth of clinical nutrition is extensive, there are many topics we have not touched upon here: research into the expanding use of ketogenic diets in different therapy areas, the dietary management of inherited metabolic diseases, the improvements in technology that have enabled further research, the list goes on.

Future innovation

The UK has been at the forefront of many of the advances in clinical nutrition and can continue to do so through further investment in research supported by responsive regulation. A recent report highlighted the need for regulatory reform to put innovation at its heart, particularly as the boundaries between food, medicine and technology become increasingly blurred.[14] With the growing body of research, we should continue to expect that nutritional care will sit at the heart of patient care. Hippocrates would be pleased.

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