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Overview

Supportive Care: An Indispensable Component of Modern Oncology

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Abstract

The advent of new cancer therapies, alongside expected growth and ageing of the population, better survival rates and associated costs of care, is uncovering a need to more clearly define and integrate supportive care services across the whole spectrum of the disease. The current focus of cancer care is on initial diagnosis and treatment, and end of life care. The Multinational Association of Supportive Care in Cancer defines supportive care as 'the prevention and management of the adverse effects of cancer and its treatment'. This encompasses the entire cancer journey, and necessitates involvement and integration of most clinical specialties. Optimal supportive care can assist in accurate diagnosis and management, and ultimately improve outcomes. A national strategy to implement supportive care is needed to acknowledge evolving oncology practice, changing disease patterns and the changing patient demographic.

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Key words: Beyond cancer; chronic cancer; definition; living with; supportive care

Statement of Search Strategies Used

A series of searches were constructed and carried out via PubMed, EMBASE and MEDLINE. This generally consisted of using phrase searching due to the specificity of the subject. Once concepts were established, the authors used Boolean operators to combine the concepts together and retrieve the most relevant papers. Once a set of results were retrieved the authors scanned each of the articles using abstract and title fields to identify key papers. Full-text access to papers were sourced via the Christie Library and Knowledge Service.

Introduction

Supportive Care Makes Excellent Cancer Care Possible
Multinational Association of Supportive Care in Cancer (www.mascc.org).

Advances in diagnosis, surgery, radiotherapy and new drugs have led to improvements in cancer survival. People

now live nearly six times longer after their cancer diagnosis than was the case 40 years ago [1]. Half of people diagnosed with cancer in England and Wales survive their disease for 10 years or more [2]. Currently in England, around 1.8 million people are living with a diagnosis of cancer and this number is increasing by over 3% a year. The total figure is set rise to over 3 million by 2030 [3].

Many more cancer patients are being treated closer to death, with novel, less toxic, high efficacy anticancer therapeutic agents developing with increasing pace within the last decade. The advent of molecular targeted agents, for example, has brought new benefits, as well as challenges, to modern cancer therapy, potentially blurring the distinction between active and palliative interventions [4].

Yet despite this significant progress, a large proportion of patients with cancer still experience morbidity and symptoms, resulting from the cancer and/or its treatment [5]. Increases in cancer incidence [6], emergency care hospitalisations [7], earlier intensive care unit admissions [8] and treatment costs [9] have all added to the global burden of cancer care. The disease is becoming a major economic expenditure for all developed countries [10]. In the UK and in the USA, cancer care costs are substantial and expected to

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rise significantly in the future due to growth and aging of the population and improvements in survival, as well as trends in treatment patterns and costs of care following cancer diagnosis [11,12].

Managing cancer and cancer treatment-related morbidity is, therefore, a significant public health and economic challenge. The coronavirus pandemic has deepened this challenge, with many cancer outpatient visits being replaced by telephone consultations, and deferral of some routine therapy, tests and procedures. This has placed additional pressures on an already fragile and vulnerable population [13]. Patients and carers are experiencing more uncertainty and anxiety associated with COVID-19. A recent study found that although patients continue to feel well supported by their healthcare teams, they have concerns about the longer-term impact of changes to aspects of their treatment. Patients and carers are no longer able to access other support services in the way that they had previously, such as hospices and peer support groups [14].

There is a growing body of evidence that timely access to supportive treatments can lead to improvements in quality of life and survival, as well as benefitting the health economy [15–17]. The development of a broad multiprofessional basis for the study and expansion of supportive care through the Multinational Association of Supportive Care in Cancer (MASCC) has been an important step in fostering the growth of an evidence base [18]. MASCC's success has undoubtedly been underpinned by successful integration of oncological and non-oncological specialties [19].

However, variations in the definition of supportive care, allocation of resources and a lack of clarity on who should lead on/provide services means that a clinical model for supportive care in cancer does not yet exist [5]. Most specialties, whilst they overlap other specialties, are based on a core of knowledge or skill that is specific to that specialty [20]. Supportive care is currently provided by a patchwork of different medical specialties, and is unique because it traverses the entire spectrum of the disease (Figure 1), from diagnosis through to survivorship or end of life care. The need for 'supportive oncology' to become a specialty in its own right is borne out not just by the progress in its development in the UK and abroad, but by the unmet supportive care need [21,22], amplified by the rising incidence of cancer worldwide, with many patients living longer with incurable illness because of more effective cancer treatments [6]. A significant next step would be to produce an evidence-based national strategy for supportive care, implemented through appointment of supportive care lead clinicians within each UK cancer centre. This, alongside support from the medical Royal Colleges and NHS England, would be fundamental in developing a sustainable clinical model.

Perhaps working as a distinct branch of oncology, 'specialists' in supportive care medicine should have the skills and resources to manage a broad range of effects associated with long-term cancers and cancer survival. This paper explores areas that are showing promise in this development, and identifies key next steps needed to recognise supportive care as an indispensable component of modern oncology.

Definition of Supportive Care

The Inuit may or may not have 50 words for snow, but supportive care seems to have that number of definitions or connotations [23]. Supportive care has been used as a euphemism for palliative care (and 'early palliative care') [24] and research suggests that a change in name (from palliative care to supportive care) results in more and earlier referrals to hospital-based services [25]. Palliative care is an integral component of supportive care, but supportive care is much more than palliative care (or even 'early palliative care').

MASCC defines supportive care as 'the prevention and management of the adverse effects of cancer and its treatment. This includes management of physical and psychological symptoms and side effects across the continuum of the cancer experience from diagnosis through treatment to post-treatment care. Enhancing rehabilitation, secondary cancer prevention, survivorship, and end-of-life care are integral to supportive care' [26].

Strategy for Implementation of Supportive Care Within Cancer Care

The potential benefits of supportive care include decreased morbidity, improved quality of life and potentially decreased mortality (i.e. secondary to optimal cancer treatment): the potential benefits for healthcare services include decreased utilisation of healthcare resources (and improved treatment outcomes) [27]. Indeed, supportive care offers patients more than many 'palliative' oncological treatments, and should be considered an essential, not just an optional, extra.

Currently, many cancer centres in the UK have supportive care services, either as a result of NHS England's Enhanced Supportive Care (ESC) Programme (discussed below) and

The supportive care umbrella

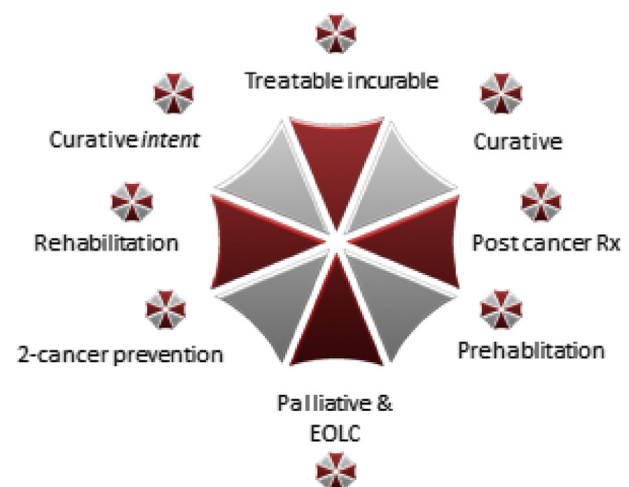


Fig 1. The supportive care umbrella

related Commissioning for Quality and Innovation (CQUIN) [28] or as a result of local initiatives. However, the format of these teams is variable, as is the patient cohort (i.e. restricted to specific cancer diagnoses) and the interventions offered (i.e. often restricted to symptom control).

Thus, a national strategy is required to standardise supportive care services in relevant settings. This needs to be evidence-based, and ensure equity of care for all cancer patients, irrespective of their cancer diagnosis or stage. The strategy needs to address the current situation, but also acknowledge evolving oncology practice (i.e. new treatments with new toxicities), changing disease patterns (i.e. cancer as 'chronic disease') and changing patient characteristics.

It needs to address education and training (discussed below) and be supported by benchmarking of services, including inspections of clinical services (incorporating patient feedback). Investment will be required to standardise supportive care services, and research funding should be allocated to determine the optimal model of care, as well as the effectiveness/cost effectiveness of the individual components of the services.

Implications for Training

Supportive care encompasses the entire cancer journey, and so necessitates the involvement of most clinical specialties, and many non-clinical services (Figure 2). Indeed, modern supportive care cannot be provided by a single clinical specialty alone. However, as with other cancer multidisciplinary teams, a dedicated 'core team' is needed to manage everyday problems, with timely input from an 'extended team' if the need arises. Importantly, the core team needs specific/ongoing education and training in principles of supportive care.

It is also important to recognise that although many supportive care services may have evolved from palliative care services, palliative care healthcare professionals generally have limited formal training in supportive care, and it is often not appropriate to extrapolate data/experience from patients with advanced cancer to patients receiving anticancer treatment, or cancer survivors. For example, the management of nausea and vomiting in advanced cancer [29] is very different from the management of chemotherapy-induced nausea and vomiting [30].

The development of specialist supportive care services must be supported by the education/training of the wider oncology workforce in the principles of supportive care (and the management of common symptoms/problems). Indeed, specialist supportive care services will only ever be able to see the 'tip of the iceberg', and so will need to focus on more complex problems (and ones requiring specialist interventions). Moreover, for example, it is much more appropriate for the team that gives the oncological intervention to manage the adverse effects of that oncological intervention.

Thus, supportive care needs to be incorporated into the curricula of all healthcare professionals involved in cancer care (including primary care physicians). Appropriate



Fig 2. The extended supportive care team

continuing professional development opportunities need to be developed for these groups. Patients and their families need access to appropriate educational resources in order to facilitate rapid/successful treatment of the complications of the cancer and/or the cancer treatment.

Enhanced Supportive Care Programme – NHS England

NHS England promoted early development of supportive care within some cancer centres via the ESC CQUIN programme. CQUIN is the framework supporting improvements in the quality of services and the creation of new, improved patterns of care [31]. ESC CQUIN was developed by The Christie NHS Foundation Trust, and was based upon six key principles for the implementation and delivery of supportive care (Figure 3) [28]. The programme developed through recognition of what specialist palliative care professionals, working alongside other cancer care disciplines, could offer across the whole cancer pathway – and through recognition of barriers to achieving earlier involvement [32]. Palliative care and supportive care are often differently organised across locations, on the basis of resources and traditions. In some centres, the two are organised as one service, whereas in others they are completely separate [33]. The ESC programme required rebranding, a closer collaboration with oncology and referral within 6 weeks of diagnosis of incurable cancer.

NHS England's Specialised Commissioning Improving Value Team worked with commissioners and clinical teams in ESC development. Fourteen cancer centres took part in the ESC CQUIN over a 3-year period (2016–2019). An interim evaluation of the scheme took place in October

2018. The programme was associated with a variety of positive outcomes, including: timelier referral of patients with supportive care needs, improved symptom control, improved quality of life, reduced 30-day mortality from chemotherapy, improved overall survival and reduced healthcare costs [15]. ESC's principles of early referral and intervention may have impacted positively on these outcomes, by better supporting patients who decide to proceed with chemotherapy, as well as those who decide not to proceed.

A limitation of the ESC CQUIN related to variation in service delivery model across the centres. Further robust research needs to be undertaken to determine the 'optimal' approach for delivery of supportive care services within cancer centres, and in other settings.

Developing the Research and Evidence in Supportive Care

When the American Society for Clinical Oncology (ASCO) celebrated its 50th anniversary, it listed the five top achievements in oncology over that period. Prominently listed was the development of highly effective antiemetic treatment [34]. What has been the impact of this key advancement in cancer supportive care, and how did we get there? Does this progress guide us in improving other areas in supportive care?

The impact of preventing emesis is broad and large. Nausea and vomiting affect all aspects of daily living: the quality of life benefits of antiemetic prevention have been documented. Economically, this advance allowed nearly all chemotherapy to be given on an outpatient basis rather than requiring hospitalisation. This also allows people to have less disruption and to remain with their families while pursuing normal activities.

These improvements are the result of thoughtful and logical research. Principles of this research included the following, which can be applied to many supportive care settings: (i) an understanding of appropriate physiology [35]; (ii) establishment of good clinical methodology [36]; and (iii) evidence that affecting specific neurotransmitter pathways resulted in major clinical benefit [37,38]. As a result of this work, 80–90% of patients can be spared emesis in difficult settings (as opposed to 0% in the past).

As we enter an era where chemotherapy is progressively less used, new areas for supportive care emerge. Are we prepared to understand in depth unanticipated challenges in supportive care? Can we prevent dermatological toxicities with tyrosine kinase inhibitor-mediated molecularly targeted approaches through better understanding of the mechanisms of these agents and skin physiology? Can we predict who is likely to have autoimmune side-effects with check point inhibitors [39]?

Skills in caring for patients with cancer, and methods of treating malignancy, continue to improve. The advances made in preventing chemotherapy-induced nausea and vomiting provide a model that can influence approaches to many other aspects of supportive care in cancer.

Interface with Acute Oncology — Ambulatory Supportive Care

Advances in cancer management continue to improve patient outcomes. This has expectedly been associated with an increase in emergency presentations with disease- or treatment-related complications. The challenges of emergency oncology presentations have led to an interest in developing optimal care models for meeting patients' needs [19]. Cancer patients seeking emergency care generally have higher admission rates, longer

6 PRINCIPLES OF ESC

1. Earlier involvement of supportive care services.
2. Supportive care teams that work together.
3. A more positive approach to supportive care.
4. Cutting edge and evidence-based practice in supportive and palliative care.
5. Technology to improve communication.
6. Best practice in chemotherapy care.



lengths of stay and higher mortality than non-cancer patients [40].

Ambulatory care is recognised as a key tenet in ensuring the safety and sustainability of acute care services. The fundamental basis for ambulatory care is that patients presenting with acute illnesses can be stratified as low risk for developing complications and therefore do not require traditional inpatient care [41].

Individualised management of acute cancer presentations is a key issue for emergency oncology services so that it can mirror routine cancer care [42]. There are an increasing number of acute cancer presentations that can be risk assessed for care in an emergency ambulatory setting. These include low-risk febrile neutropenia, cancer-associated deep vein thrombosis, incidental pulmonary embolism, chemotherapy-related acute kidney injury, chemotherapy-induced nausea and vomiting, indwelling line infections, acute management of pain crises, malignant hypercalcaemia and other electrolyte abnormalities, asymptomatic brain metastases and malignant pleural effusion [43–46].

Ambulatory models offer the opportunity to integrate palliative care and supportive care with oncology and acute services. This facilitates improved access for patients to expertise in cancer care and immediate management of the complications of cancer treatment, with the goal of preventing downstream complications and future emergency presentations. For example, ambulatory enhanced supportive care models have shown utility in the management of low-risk febrile neutropenia [17].

Modelling of ambulatory emergency oncology services within integrated supportive care services is therefore key in the provision of high-quality, personalised and sustainable emergency oncology care.

The Importance of Supportive Care in Experimental Cancer Medicine

Experimental cancer medicine trials (ECMTs) are fundamental to the development of novel cancer therapies. The primary aims of ECMTs are to identify treatment-related toxicities and determine the recommended drug dose [47]. These trials are increasingly complex [48], intensive, with risks of toxicity for patients, but there is a growing recognition that they are a valid therapeutic option [49].

ECMTs have strict eligibility criteria, with the need for patients to have a performance status of 0 or 1, indicating high levels of day to day functioning [50]. However, these patients typically have advanced disease, multiple previous lines of treatment and, therefore, a high associated symptom burden [51]. Hui *et al.* [52] found that patients referred for ECMTs have a similar symptom burden to those who were not, despite the perception of higher levels of fitness. A high symptom burden has also been associated with early discontinuation from trials [53], highlighting the potential role for supportive care. Brédart *et al.* [54] suggested that this patient group is more likely to accept increased toxicity

to facilitate continued access to trial drugs. In one study, ECMT patients stated that they would still participate in a trial despite the potential risk of serious toxicities and a 10% chance of death [55].

Research suggests that ECMT patients are less inclined to accept traditional palliative care due to a general, and sometimes unrealistic, optimism regarding trial participation [56], alongside the perception that palliative care is only applicable at the end of life [57]. However, supportive care practices within the early phase trials setting have the potential to reduce the impact of symptom burden and adverse events on patients [52], potentially increasing trial recruitment and the length of time patients spend on an experimental therapy. Evidence in an ongoing study by Ferrell *et al.* [58] indicates that additional support can improve the quality of life for this patient group. On top of the benefit to patients of access to additional therapies, prolonged exposure to trial drugs supports research through increased numbers of evaluable patients, aiding efficient and accurate assessment of novel therapies. Thus, there is growing evidence for the role of supportive care for ECMT patients with the need for increased research to assess potential benefits and identify optimal routes for its delivery.

Learning from Other Countries: Implementation of Supportive Care in France

With the aim of increasing and improving community investment in supportive care, MASCC is promoting several different approaches to engage countries, such as:

- The creation of accreditation for hospitals with dedicated supportive care units;
- Promotion of MASCC and collaboration with local associations at MASCC meetings
- Special links with these associations, such as joint memberships.

France committed to the supportive care approach at the end of the 1990s and as part of its first cancer plan in 2005. The French Speaking Association for Supportive Care in Cancer (AFSOS), affiliated to MASCC, was created in 2008 with the objectives of:

- Promoting knowledge and execution of supportive care in oncology;
- Sharing experience with all professionals involved in the accompaniment and care of symptoms throughout all phases of the disease;
- Identifying and understanding the impact of the transferability and interdependency between disciplines: facilitating key aspects, obstacles, interests and limitations of work;
- Heightening ethical awareness among medical staff.

AFSOS has set up a research committee with four strategic priority directions: healthcare organisation (cross-

disciplinary meetings and departments, supportive care units, dedicated teams), management of cancer symptoms and treatments, health behaviour and human and social sciences.

Its actions are targeted towards institutions (e.g. The French National Cancer Institute, Ministry of Health), professionals (guidance and symposia on specific topics such as emesis or nutritional disorders), as well as patients and their specific associations (through a patient-facing website, a roadshow truck crisscrossing France and an inventory of supportive care resources). AFSOS has developed national meetings devoted to physicians and nurses, physiotherapists or other health caregivers. Guideline resources (with a toolkit app) are discussed during a specific 2-day event and updated every 2 years. AFSOS is involved in promoting international collaboration with other MASCC-affiliated societies (e.g. Network Italiano Cure di Supporto in Oncologia [NICO] and the Japanese Association of Supportive Care in Cancer [JASCC]).

This French national mobilisation has led many regional teams to get involved in cancer safety management projects for the benefit of patients and their relatives and can be copied in other countries.

Interface with Other Specialities (e.g. Endocrinology and Diabetes)

Optimal supportive care of cancer patients requires input from a range of specialties outside of oncology to assist accurate diagnosis and management, and ultimately improve outcomes.

Up to 25% of inpatients with cancer have diabetes or are at risk of diabetes from the treatments they receive [59]. The importance of this is increasingly recognised; patients with diabetes and cancer have an increased length of hospital stay [60] and mortality [61]. Although there is currently a lack of data demonstrating that improving glycaemic control reduces mortality for cancer patients, it is certainly true that effective and timely management of hyperglycaemia improves quality of life and reduces inpatient length of stay, but this requires specialist input from a diabetes team.

Similarly, up to 40% of inpatients with cancer experience hyponatremia, commonly secondary to syndrome of inappropriate antidiuretic hormone secretion, although in the era of immunotherapy, cortisol deficiency is an important and increasing cause, which can be fatal if missed [62,63]. Untreated hyponatremia can delay oncology treatments and extend the length of hospital stay [64]. Diagnosis and management of hyponatremia is poorly managed in general, and the oncology population are no exception [65]. We consider expert supportive care input into the management of hyponatremia in oncology patients to be essential in improving this situation.

Fractures, particularly those of the hip and spine, are devastating, with up to 30% mortality at 1 year following hip fracture and significant ongoing morbidity. Vertebral fractures are highly predictive of further fracture but reporting

of these is poor in the UK [66] and there are a number of reasons why this may be even lower in an oncology setting [67]. The risk of poor bone health and fracture is increasingly recognised across a number of malignancies; for example, a recent large Danish registry study showed increased risk of fragility fracture in adults with haematological malignancy, with the largest risk in the first 2–4 years following initiation of treatment [68]. Given the devastating nature of fractures, there is much supportive care work to be done to identify and treat at risk patients and manage fragility fractures effectively across the spectrum of the cancer journey.

Endocrinologists have had a traditional role in cancer survivorship [69]. For example, managing the long-term effects of brain radiotherapy on the pituitary gland in childhood brain tumour survivors. As the prognosis for adult brain tumour survivors improves, similar issues may arise [70]. More recently, endocrine toxicities, such as hypophysitis and insulin-deficient diabetes caused by immunotherapy treatments, are also keeping endocrinologists busy [63] in collaboration with acute oncology [71]. This will become an even more complex issue as immunotherapy moves into the adjuvant arena, with expert input into decision making algorithms crucial [72].

Discussion

The current focus of cancer care is on initial diagnosis and treatment, and the last year of life (end of life care) [73]. However, a large proportion of patients with cancer experience debilitating morbidity and complex symptoms, resulting from cancer and/or its treatment across the entire cancer journey. Supportive care has been shown to improve quality of life, symptom burden and survival, as well as benefitting the health economy [15–17]. Thus, supportive care should be an integral component of modern oncology management and should involve input from a range of specialties within and outside of oncology. Furthermore, its continued development, perhaps most effectively as a subspecialty of oncology, is essential in supporting advances in oncology and the changing demographic of the cancer population.

Conflicts of interest

R. Berman is a director of Supportive Care (UK) Ltd. This is outside the scope of the submitted work.

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