The declaration of the War on Cancer defined a new frontier in an extended battle against a formidable adversary, whose presence has pervaded throughout human history. In 1971, US President Nixon signed the National Cancer Act at a time of renewed hope and collaborative commitment towards seeking a definitive cure for cancer. Forty years on, and the battle continues.

To consider how far we have come, first we must know our enemy. Cancer is a perplexing opponent. Over a hundred distinctive anatomical and histological disease subtypes are known collectively as cancer. There are molecular variants within subtypes of malignancies of a single organ, with differing prognosis, metastatic potential and response to treatment. Its arcane nature is reflected in its complex genetic and biochemical pathways, cell survival mechanisms and processes of proliferation and dissemination. It is never a static challenge. Its inherent genetic instability, evolution and resistance undermine our immune system and the artillery of treatments available.

Worldwide, the past 40 years have seen over $200 billion invested into cancer research and over 1.56 million research publications. These efforts have procured remarkable advances in our understanding of cellular biology and molecular genetics. The sequencing of the human genome and molecular profiling have propelled recent successes with isolated targeted therapies, and provides a strong foundation for future treatment modalities. However, for most common cancers, this has translated into, at best, modest improvements in cancer survival. At worst, perhaps treatment attempts may even be to the detriment of patient’s quality of life?

Health related Quality of Life (HRQOL) is a multidimensional construct, which is beneficial in evaluating the progress of achieving health outcomes across different segments of the population. It encompasses the physical, emotional, social and behavioural aspects of wellbeing, as subjectively perceived by a person depending on their value system and cultural context. Psychological aspects include subjective distress, satisfaction with treatment, existential issues, relationships and the impact of illness on sexuality and body image, which are all considered in measuring the efficacy of medical interventions. Commonly used measures are the Rotterdam Symptom Checklist, SF-36 and the FACT-G, as standardised HRQOL measures are being adopted in the evaluation of cancer therapies.
The need to balance survival and quality of life is particularly pertinent to us. In Australia, cancer is one of the leading causes of mortality, and has surpassed cardiovascular disease as our greatest disease burden\textsuperscript{14,15}. Within their lifetime, 1 in 2 men and 1 in 3 women will develop cancer\textsuperscript{16}, with incidence rates expected to rise by 30\% over the next decade as the population ages\textsuperscript{17}. Over the past 25 years, the nation’s age standardised cancer mortality rate has decreased by 16\%, with fewer deaths for most common types of cancer\textsuperscript{15}. People with cancer are now living longer. With a greater number of cancer survivors, there is a crucial need to address issues of quality of life\textsuperscript{18}.

The need to move beyond Ehrlich’s enduring concept of ‘magic bullets’ has long been recognised\textsuperscript{19}. A shift in strategy requires numerous fronts within the continuum of primary prevention, early detection, diagnosis, treatment, survivorship and palliation. This essay will explore the advances within this spectrum over the past 40 years, with particular attention to the ways in which they have affected quality of life for Australians living with cancer.

**THE SPECTRUM OF CARE**

*Prevention and early detection*

Carcinogenesis occurs insidiously over decades. Clearly, the optimal time to intervene is while the offending cells are premalignant and asymptomatic, or premetastatic. Evidence affirms the reductions in cancer incidence and mortality are primarily attributed to effective prevention and appropriate screening\textsuperscript{3,6}. Early intervention carries a far better prognosis, and avoids or minimises the severity and distress of a patient’s experience\textsuperscript{14}.

Prevention is pivotal, as the absence of disease maintains favourable HRQOL. The shining beacon of cancer prevention has been immunisation, with widely successful campaigns for HPV and HBV protection\textsuperscript{20}. Alas, preventive medicine also recognises that we can be our own worst enemies. Well aware of the health risks, social and genetic influences contribute to an individual’s decision to engage in unhealthy behaviours. A third of cancer deaths in Australia are attributable to known modifiable risk factors\textsuperscript{15} - smoking, poor nutrition, physical inactivity, obesity, alcohol misuse and excess exposure to ultraviolet radiation\textsuperscript{14}. This is a particular problem amongst the Indigenous population who have a greater propensity to cancers with poorer outcomes, such as lung and head and neck cancers, due to higher rates of smoking and obesity\textsuperscript{21}. 


With the preponderance of cancer and chronic disease rising\textsuperscript{14}, the exigency for policy and reform requires multi-sectoral interventions involving government, public and private sectors and communities. A monumental victory has been successes with tobacco control, but the struggle continues with the behemoths of the tobacco industry. The existing knowledge must be supported by establishing environments that are conducive to healthy living, in which healthier choices become easier choices, thereby ensuring a better quality of life.

Whilst primary prevention is essential, some cancer risk factors are simply not modifiable. We cannot change our age, our genes or our family history. In such instances, population based screening programs have allowed for earlier detection for breast, colon and cervical cancer. High risk groups, such as those carrying a BRCA-1 or BRCA-2 mutations receive intensive screening, and in some cases, prophylactic intervention\textsuperscript{14}. Such strategies have been vastly successful. So too have we increased public awareness of melanoma and prostate cancer. Prevention may not be better than a cure, but in the absence of Ehrlich’s silver bullet, prevention and early detection is paramount. We have come a long way in forty years of cancer research, but perhaps our greatest success has been the increase in knowledge of cancer risk factors coupled with preventative approaches to avert or minimise incursions to HRQOL\textsuperscript{14,20}.

**Diagnosis and Treatment**

Cancer is a diagnosis embellished with fear. Conspicuous lumps, suggestive symptoms or a family history unleashes a torrent of thoughts and fears of receiving the bad news. The stigma associated with cancer once drove patients to hide their illness. With the belief that there was no cure, then perhaps it would be easier to deny its presence, at the detriment of delaying possible treatments or symptomatic relief. The public image of cancer is thankfully now one of acceptance and support, as attitudes adapt to the possibility of multiple treatment modalities.

With increasing access to information and a shift from paternalism towards a shared decision making process between patients and doctors\textsuperscript{22}, patients are in a greater position of ownership over the course of their treatment. Often as a terminal malady, the disease itself may yield the greatest power, but the patient still has the choice to determine how they will carry themselves and the extent to which they will battle. Higher HRQOL can be expected through greater treatment satisfaction, acceptance and clarity for their journey.

Every case is considered individually, as specialists collaborate to determine the right treatment for the right patient at the right time\textsuperscript{23}. HRQOL has exponentially improved in advanced cancers with curative potential (germ cell cancer, SCLC, ovarian cancer, choriocarcinoma, lymphoma
and AML&ALL. For most remaining cancers, gains in HRQOL are seen with stable disease and remission. HRQOL has improved even for highly aggressive opponents, such as pancreatic cancer, despite treatment not extending survival. Surgery, radiotherapy and systemic therapy are the mainstays of treatment.

**Surgery**

Surgery for malignancies has transformed over decades, and is almost unrecognisable from the desperate and borderline barbaric excisions recorded thousands of years ago. Scans and biopsies have replaced the need for extensive exploratory surgery. Technological advances, innovative surgical approaches and the neo adjuvant and adjuvant treatments have allowed for less invasive processes. Robotic surgery in urology and otolaryngology extends human abilities, providing precision and access with minimal disruption to surrounding structures. Regardless of whether a tumour can be cured or more effectively palliated with surgical resection, HRQOL improves with better aesthetic outcomes and preserved organ function. Reduced recovery time and rehabilitation have also dramatically improved surgical outcomes, and thus also HRQOL.

**Radiotherapy**

Various radiotherapy options harness powerful energy to target cancer cells. The collateral damage to normal tissue results in an array of early and late side effects. Developments such as stereotactic radiosurgery and proton beam radiotherapy aim radiation to minimise the damage to normal tissue while delivering a high dose to the cancer. Amifostine is currently the only radioprotector, used to prevent xerostomia in head and neck radiotherapy.

**Systemic therapy**

Chemotherapy development has always been challenged with genetic diversity and resistance so synergy between a drug and malignancy can never be predicted with absolute certainty. Furthermore, animal models were unreliable and subsequently fewer than 10% of clinically trialled drugs were approved between 1970-90. The approved drugs, such as taxanes, anthracyclines, paclitaxel and platinum compounds were applied in assorted combinations. For the fortunate few patients, some advanced cancers were cured; for others, adjuvant therapy brought disease-free or progression free survival, with fewer negative side effects. For those who received no benefits from treatment, chemotherapy may have caused needless toxicity.
The dichotomy of benefits and shortcomings of cancer treatments provides a compelling rationale for measuring HRQOL. Vivid depictions of early chemotherapy resonate with a sense of despair, as patients endured the unavoidable toxicity of vigorous therapy cycles. At times, the severity of dose limiting nausea and vomiting, neuropathy and bone marrow suppression can exceed the disease symptoms. Further, fatigue and psychosocial symptoms can be difficult to distinguish from cancer symptoms. Progress has been achieved in controlling adverse effects through the use of colony-stimulating factors and chemoprotective agents which enable higher dose regimes. Administration is safer and easier with indwelling intravenous catheters. Antiemetics, platelet and red cell transfusions and broad spectrum antibiotics have brought some relief, but the acute and chronic effects of the drugs remain a challenge.

Adverse effects from therapies can be minimised by identifying patients that are likely to respond to a specific treatments. For hormone therapy, oestrogen-receptor-positive breast cancers benefit from tamoxifen. Genomic and molecular profiling of signalling pathways have beckoned a promising era of targeted therapy. The landmark discovery was Imatinib, a BCR-ABL tyrosine kinase inhibitor (TKI) which targeted CML’s unique single molecular pathway. Other TKI inhibitors followed for gastrointestinal stromal tumours, renal cell and hepatocellular cancer; improving the HRQOL and overall survival by 3-12 months in a palliative setting.

The translation of discoveries to a clinical reality depends upon the willingness of patients to enrol in clinical trials. In Australia, close to 4-6% of newly diagnosed cancer patients are enrolled in various stages of collaborative and pharmaceutical clinical trials. For some, participation may enable higher quality care and access to new treatment options, but there is limited high quality evidence indicating overall improved outcomes. HRQOL measures are incorporated into most clinical trials, and in 2010 the Australian Cancer Trials website (ACTO) was launched to centralise trial recruiting information for patients and doctors.

Survivorship

Cancer challenges every aspect of self and identity. Survivorship centres upon enhancing the quality of life of patients and their families ‘living with, through and beyond a diagnosis of cancer’. Australians are fortunate to receive among the best comprehensive cancer care in the world. Public and private health services are responding to meet the holistic needs of patients. Following treatment, long term symptoms or late onset complications may require further evaluation and management. Rehabilitation, health promotion and psychosocial care improve the quality of ongoing care.
The tyranny of distance unfortunately still causes a divide in cancer care for rural populations. Out of pocket expenses for patients contribute to suboptimal decisions and non compliance with treatments, and financial distress adversely impacts on patient’s recovery and HRQOL. In Queensland, the mortality risk for rectal cancer patients increases by 6% for every 100km in distance they live from a radiotherapy centre. The disproportionate burden is further reflected in NSW rural Indigenous populations, as they are three times more likely to die from some cancers than those living in urban NSW areas. Delayed diagnosis and poor availability of screening services, lifestyle factors and lack of funding are contributing factors to higher mortality rates and poorer HRQOL. Strategies are being investigated, and increases in travel and accommodation assistance for regional cancer patients has been seen.

**Palliative medicine**

As a profession, medicine is innately fixated on curing and prolonging lives. There is an aversion to death, as it seemingly signifies failure and defeat. The vigorous determination to treat was challenged by Cecily Saunders, with the opening of an end of life care hospice in 1967. In the 1970s, patients would spend their numbered days on the oncology ward. It was a place of anxiety and anguish, as pain relief was withheld for fears of dependence and deterioration. There was strong resistance to palliative care and it wasn't until the 1980s that it was accepted as a fundamental discipline of treatment.

Palliative care has profoundly shaped cancer treatment and HRQOL by restoring the holistic care and dignity of patients. The knowledge acquired on cancer pain management owes much to the clinical trials that have stemmed from this discipline. This has benefitted almost all cancer patients as up to 90% of patients experience pain at differing stages of illness. In the face of terminal illness, 60% of cancer patients are referred to palliative care services. Pain and symptom relief, psychosocial and spiritual attention allows them to rest in comfort and peace.

**MEDICAL EDUCATION**

In some capacity, almost all medical graduates will be involved with the care of cancer patients. Although a continually shifting field, the principles within the continuum of care will remain the same. The objectives outlined by the Cancer Council Oncology Education Committee provide a comprehensive foundation on which further knowledge can be built upon. An understanding of quality of life, its measures and impact on therapeutic ratios will equip future health professionals in making the most appropriate treatment decision. Clinical experiences are
valuable learning opportunities. Students will gain an insight into a patient’s journey if they spend time with them, hear their story, appreciate the input of multidisciplinary care and observe the interaction of patients and their doctors as they share in the hopes and anguish that accompany such a formidable illness. Interests in research, epidemiology, public health and other oncology related fields should be encouraged.

CONCLUSION

The burden of cancer is far reaching. It challenges and reshapes all the domains of an individual’s quality of life. Over the 40 years of the war on cancer, progress has certainly been made. “Every era casts illness in its own image” Perspectives are seen through the light of its current understanding. Previously viruses held the answers. Now our focus is on genetics and the interplay between immunology, gene regulation and the microenvironment. In the midst of these shifts, the one common factor is the importance of each individual battle. Perhaps it is essential to redefine the war, and emphasise quality over cure.
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