“40 years after the war on cancer – How far have we come?”

Introduction

Four decades ago, American President Richard Nixon signed the National Cancer Act, directing attention, and more importantly, government funding, towards the need to research and find a treatment for cancer to make the “conquest of cancer a national crusade”\textsuperscript{1,2}.

This act proved to be the impetus for significant advancements in cancer research and treatment, paving the way for numerous groundbreaking achievements in the field of oncology\textsuperscript{3}.

More than 60\% of people with cancer will now survive at least five years after diagnosis, and the mortality rate of cancer has decreased 16\% in the past two decades alone\textsuperscript{4,5}. New drugs are able to treat cancers and extend the lives and survival rates of its patients, and vaccines have been created that can prevent the development of certain forms of cancer\textsuperscript{6}. The use of multimodal therapy has reduced the need for radical surgeries, and the development of personalised cancer treatment has allowed for more targeted and effective approaches to treatment\textsuperscript{7,8}.

However, cancer continues to be a leading cause of death and burden of disease, and locally, 1 in 2 Australians will be diagnosed with cancer by the age 85\textsuperscript{9}.

This essay will discuss the progress that has been made in understanding the role of human genomics in cancer, the evolution of cancer care with regard to prevention, advancements in screening, detection and treatment, the evolving role of the health professional in cancer treatment, and the future direction of cancer therapy and research, with the ultimate goal of eliminating cancer as one of the biggest health challenges that faces us today.
Progress in the genetic understanding of cancer

The focus of cancer research has broadened considerably over the years. Scientists now have a greater appreciation of how a patient’s individual genetic makeup can affect their chances of developing a variety of cancer, and its subsequent severity and response to treatment, reflecting the importance of understanding the entire spectrum of factors that contribute to the development of cancer\textsuperscript{9}.

Research has led to the discovery that mutations that have occurred in our genes are the cause of most, if not all, types of cancer. One of the most significant advances towards this was with the completion of the Human Genome Project, which allowed for the identification of more than 290 genes that relate to the causes of various cancers\textsuperscript{10}.

The identification of these gene mutations has uncovered two key classes of cancer genes: oncogenes – genes that often drive the uncontrolled cell growth phase which is a hallmark of cancer, and tumour suppressor genes, which in normal states preserve the integrity and normality of the genome\textsuperscript{11}. In cancerous states, these gene classes have mutated and are unable to function in an appropriate manner, and by Darwinian evolution, develop a survival advantage with the potential to proliferate autonomously, invade tissues, and metastasise to distant sites\textsuperscript{10}.

Understanding that the changes in an individual’s genes provides the catalyst for cancer initiation and development means that we are better equipped than ever before to design therapies that specifically target the molecular defects of the tumour. This principle can be extended to incorporate all domains of cancer management, from developing preventative measures, facilitating earlier detection and screening of disease of at-risk populations; to monitoring treatment responses and predicting patient outcome and prognosis based on their genotype\textsuperscript{12}.
Advances in cancer prevention

An important shift in cancer research that occurred was to understand the causes of cancer and develop strategies to detect it and intervene early, or to prevent its onset completely\(^{10,13}\). Some of the most significant reductions in mortality rates have come from the application of preventative health measures and health promotion campaigns, based on the knowledge of common causes of cancer\(^{14}\).

Numerous studies have identified a link between lifestyle factors such as smoking, poor diet, physical activity, body weight or composition and their role in both the development and recurrence of certain cancers, and the identification of the carcinogenic effects of certain environmental and occupational exposures has resulted in important changes in preventive interventions and public policy\(^{10}\).

Changing the incidence and mortality of cancer can be accomplished by investing funds into behavior modification and health promotion and education campaigns\(^{10}\). Since the establishment of the causal relationship between tobacco use and lung cancer, measures to combat cigarette smoking such as media campaigns, law changes and restrictions on public smoking areas have all contributed to reducing rates of smoking and mortality from lung cancer, illustrating the success of public prevention strategies in cancer management\(^{15}\).

Infection-associated tumours comprise nearly 20% of all cases of cancer worldwide, and the development of vaccines in preventing bacterial or viral infection has played a significant role in reducing the morbidity and mortality of these diseases\(^{16}\). The hepatitis B vaccine was the world’s first cancer prevention vaccine, preventing the progression of chronic infection to hepatocellular carcinoma\(^{15}\). And the development of a prophylactic vaccination against human papillomavirus 16 and 18 means that 70% of cervical cancer is now preventable\(^{17}\).
Advances in screening and early detection

The purpose of screening an asymptomatic individual to detect early evidence of an abnormality is to recommend preventative strategies or treatment that will provide the patient with a better health outcome than if the disease had been diagnosed at a later stage. Most cancers have a pre-invasive or precursor stage, and researchers have identified this ‘window’, during which it is possible to detect and treat the disease before it reaches an advanced, symptomatic stage, and this forms the basis for screening\(^15\).

Nationwide screening programmes have been applied in Australia for the early detection of breast cancer, colon cancer, and cervical cancer, amongst others, to great effect. Studies consistently demonstrate that the implementation of these programs is beneficial in reducing cancer mortality rates, and cost effective for society\(^10\).

Routine mammographic screening in women aged 50-69 years has reduced the risk of dying from breast cancer by 25%, and screening for cervical cancer using the Pap test for detecting pre-cancerous cervical lesions has the potential to reduce the incidence of squamous cell carcinoma of the cervix by up to 90%\(^18,19\).

Currently, not all cancers are amenable to screening, and so the focus of future cancer research should be towards developing molecular biomarkers and tools that will allow us to identify markers of disease at an earlier stage of disease, and ultimately provide patients with a better chance of survival\(^10\).

Advancements in cancer treatment

The cornerstone of cancer treatment revolves around a triad of chemotherapy, surgery, and radiation therapy, and the past four decades
have been host to important advances in these treatment specialties, as well as the expansion of supportive or palliative care\textsuperscript{10}.

\textit{Advances in chemotherapy}
Despite the side effects often associated with chemotherapy, these drugs have dramatically increased the survival rates of cancer patients, to the point that some cancers are now curable in the majority of patients\textsuperscript{10}. Gleevec, a drug that targets a chromosomal defect found in most chronic myeloid leukaemia cases, has transformed this disease from a death sentence into a chronic, manageable condition with a 5-year survival of 95\%\textsuperscript{20}.

\textit{Advances in surgery and radiotherapy}
Continual refinement of surgical procedures over the past decades has culminated in fewer disfiguring surgeries for patients with less damage to surrounding normal tissue and structure, faster healing times, improved post-surgical cosmetic results and improved recovery\textsuperscript{10}.

The use of adjuvant and neo-adjuvant chemotherapy or radiotherapy has similarly allowed for greater preservation of normal structures, best evidenced by clinical trials showing that a lumpectomy with radiation is as effective as a radical mastectomy in the treatment of breast cancer\textsuperscript{21}.

Radiotherapy, with its computer-guided precision, now allows for intensely focused doses of treatment to cancerous areas with less damage to surrounding tissue. It has also provided therapy for cancers in areas that were previously inaccessible to surgeons, becoming widely used in the domain of head and neck cancers\textsuperscript{22,23}.

\textit{Advances in supportive care}
The development of supportive care therapy has allowed treatment to become safer and has minimised the toxicities and side effects associated with cancer therapy.

An increased understanding of pain management and mechanisms of pain in cancer patients has led to a wider use of multimodal analgesic use, drastically improving quality of life issues for patients at all stages of
treatment\textsuperscript{24}. Anti-emetic use has improved the tolerability of chemotherapy by reducing the incidence of nausea and vomiting, and the administration of haematopoietic and colony-stimulating growth factors to replenish depleted red and white blood cell levels in the bone marrow has reduced the incidence of severe infections that were once a common side effect of cancer treatment\textsuperscript{25}.

**Changes in the medical approach to patient management**

The traditional concept of cancer management, with the malignant disease being managed by a single discipline, has largely been replaced by a multidisciplinary team approach\textsuperscript{26}. There has also been a shift towards a more holistic approach to patient management\textsuperscript{27}. Doctors must be aware of the different emotional and psychosocial aspects of malignant disease with which the patient must contend, as understanding the patient’s thoughts regarding their diagnosis is pertinent to achieving a successful doctor-patient relationship\textsuperscript{10,28}.

**Medical student education and knowledge**

The importance of quality cancer education for medical students must not be overlooked. In Australia, cancer remains one of the leading causes of death in society, however, improvements in survival rates of cancer patients means that there are now more people who have been affected by cancer than ever before. It is therefore incumbent upon students to be armed with current, relevant and comprehensive knowledge, as well as develop appropriate skills and attitudes to interact with cancer patients and survivors\textsuperscript{29}.

Complete medical cancer education should incorporate aspects of cancer control (epidemiology, prevention, screening), clinical skills, patient communication skills and palliative care into the medical curriculum. Medical student learning has changed to predominantly problem-based and self-directed learning in response to a vast increase in the amount of medical
knowledge of cancer and the shift in patient expectations of the medical profession\textsuperscript{26}.

As oncology develops into a multidisciplinary specialty requiring the input of multiple medical and surgical units, medical students are coming across aspects of cancer management in an ever-increasing pattern throughout the curriculum. The development of an Ideal Oncology Curriculum by the Cancer Council Australia has identified \textit{Five Essential Cancer Clinical Experiences for Medical Students}; with the purpose of ensuring students have insight into a patient’s perspective regarding the diagnosis of cancer and its management, whilst ensuring that oncology learning remains relevant in its clinical context\textsuperscript{28}.

\textbf{The future direction of the “cancer crusade”}

Our current society has now reached a defining moment in our efforts to treat and cure cancer. The increasing number of cancer patients and survivors will test the capabilities and infrastructure of our healthcare system as physician shortages arise\textsuperscript{30}. Despite this, the advances that have been made into the understanding of cancer place us at an exciting moment in cancer development timeline, as we witness a shift towards personalised cancer treatment.

\textit{Increasing demand for care}

An aging population, improved screening and detection rates, and more effective cancer treatment have culminated in a steadily increasing number of cancer patients and survivors\textsuperscript{31}. New cancer therapies may prolong survivorship, however, lead to treatment-related medical problems or require ongoing surveillance, ultimately leading to an overall greater utilisation of health resources per patient per unit of time\textsuperscript{32}.

In light of the increasing requirements of cancer patients, studies predict that the number of clinical oncologists will soon become insufficient to meet the needs of cancer patients in the community\textsuperscript{33,34}. Appropriate care is imperative during the patient’s transition from active treatment to follow-up
and surveillance, and so new, innovative models of care may be required to alleviate the workforce deficiency in oncology specialists. Collaborative practice models, with the use of “physician extenders” – trained nurse practitioners or physician assistants, or general practitioners, may require these health professionals to assume a greater role in the ongoing care of the recovering cancer patient.\textsuperscript{35,36}

\textit{The cost of cancer care in Australia}

The economic expenditure involved in cancer research and care continues to grow as the burden of disease increases in developed countries. In Australia, cancer costs more than $3.8 billion in direct health system costs, with a markedly even greater cost to the economy once the losses due to premature death and disability are considered.\textsuperscript{9,37} Greater emphasis is required in primary prevention and treatment strategies to ensure that the most effective approaches are being utilised in cancer care.

\textit{Continued collection of cancer data}

Service providers, researchers, health administrators and government sectors require consolidated information on the burden of cancer in the community. It is important to ascertain how cancer and its risk factors affect different populations, how it is being managed, gaps that may exist in the availability and accessibility of services within communities, and the effect of government policy initiatives on cancer outcomes.\textsuperscript{38}

\textit{The era of personalised medicine}

The use of non-specific, non-targeted therapeutic agents against a broad variety of tumours has largely been overtaken by an approach in which cancer treatment and prevention strategies are based on both a person’s genetic makeup, and the genetic determinants of the cancer itself.\textsuperscript{31} This concept of personalised medicine has the potential to maximise the efficacy of cancer treatments whilst simultaneously minimising its toxicity and side effects, as we choose therapies specifically targeted towards the molecular defect. Knowledge of certain defects in a cancer will also allow identification of
populations high-risk for a certain cancer type, strengthening our efforts in cancer prevention, screening and early detection\textsuperscript{10}.

**Conclusion**

The advances that have taken place in the last 40 years into the understanding of cancer at the basic, molecular level have resulted in significant progress in the field of oncology. The use of personalised cancer medicine has replaced a one-size-fits-all treatment model, and our approach to the management of the cancer patient has also changed in this time. Emphasis has shifted towards the multidisciplinary approach with multimodal treatment and supportive therapy, with more directed efforts towards prevention, screening and early detection of these cancers.

However, with sustained population growth and Australia’s aging community, the burden of cancer continues to grow, and this remains a major test for developed countries. The challenge that faces us is to sustain clinical research, support and funding in order to improve the entire spectrum of cancer care. The good news is that the significant advances that have already been made into the understanding of cancer position us to make even greater discoveries in the coming years.
References


