



Can We Afford to Live Longer?

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Looking at the title of this article, one could be forgiven for thinking that it deals with retirement planning or financial provision for “the golden years”. However, potentially high health costs are involved in surviving to a ripe old age, which may well have an unexpected impact on retirement plans and savings.

It is well documented that the mortality improvement that occurred in developed countries in the 20th century was quite remarkable.¹ This improvement has been ascribed to progressive economic development that produced better housing, sanitation and hygiene and control of many infectious diseases. It is generally accepted that socioeconomic status is inversely related to health status; this applies on both an individual and a national level.

Progressive economic growth delivers investment in healthcare and programmes that address health at varying levels. These include primary prevention, screening, and tertiary health facilities with advanced diagnostic and therapeutic capabilities. With the direct investments in health come regulations regarding workplace safety, environment control and food quality assurances. Resources become available to promote healthy living, including smoking cessation and healthy eating and lifestyle choices. Greater infrastructure can be available for caring for the ageing population and attending to their healthcare needs.

Surprising variation in mortality

While long-term trends of improved mortality may parallel economic improvement, mortality rates can increase in times of rapid growth, surprisingly enough. This may relate to the stresses involved in rapid development of companies and technologies not only producing their own stress environments but causing competitor companies to fail. Increased mortality appears to relate to work stresses, injuries and cardiovascular illness.²

Because the major advances in mortality reduction have already been made in the developed countries, further improvements in mortality require far more emphasis on sophisticated healthcare. Not surprisingly, therefore, low-income countries at present have greater rates of improvements in mortality than high-income countries, as they attend to the provisioning of basic services and healthcare.

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About This Newsletter

Risk Insights is a technical publication produced by Gen Re for life and health insurance executives worldwide. Articles focus on actuarial, underwriting, claims, medical and risk management issues. Products receiving emphasis include life, health, disability income, long term care and critical illness insurance.

The contribution of infectious disease to mortality has varied over time. Low-income areas still experience a significant impact of diarrhoeal disease, tuberculosis, malaria and HIV/AIDS.

Dr. William H. Stewart, the U.S. Surgeon General from 1965 to 1969, reportedly said, “It is time to close the book on infectious diseases and declare the war against pestilence won”. Even if he never actually said it, the remark is often quoted and reflects the prevailing belief at the time that infections posed no future threat.

Since then, the rise of antibiotic resistance and new infectious threats, such as HIV and H5N1 influenza, have brought about the realization that unpredictable epidemics have the potential for significant and even catastrophic impact. Newer antibiotics and anti-viral agents come at a significant cost but are used for limited periods.

Impact of changes on cardiovascular disease and cancer

The major contributors to mortality in developed countries have been cardiovascular disease and cancer. In recent years, however, cardiovascular death rates have fallen with the introduction of stricter cholesterol and blood pressure control, together with smoking cessation and the culture of health and exercise. Medications for cholesterol and blood pressure control are inexpensive and freely available. The development and widespread availability of interventional cardiology has had a major impact on the management of coronary artery disease. No one would pretend that invasive cardiology and cardiac surgery are inexpensive. However, the costs are predictable and controllable, and usually are a once-off intervention. The death rate from stroke has also decreased, a trend that will continue, though absolute numbers may not drop as impressively because of the increasing number of elderly people.

In the U.S., cancer has recently become the most common cause of death. The management of cancer has predictably become far more complex and sophisticated. In order to reduce the cancer burden, prevention would seem the most appropriate intervention. Even greater smoking cessation, for example, would dramatically drop cancer incidence.

Another example would be the introduction of human papilloma virus (HPV) vaccine, which could almost eliminate cervical cancer. Early detection of cancer has been thought to predict better outcomes, as the earlier it is found, the more likely it may be cured. There is indeed evidence that introduction of certain screening programs, such as the Pap smear and mammography, have reduced cancer mortality.

Most screening has proved disappointingly unsuccessful, since many of the cancers detected are relatively benign and unlikely to have an impact on mortality.³ Indeed, the investigation of these tumours can cause more harm and suffering than if the disease had remained undetected. The development of biochemical markers and the detection of circulating cancer cells and cancer DNA promises to allow even earlier detection of tumours but interpretation of these tests remains problematic. Despite already finding a place in cancer monitoring, for the foreseeable future they are unlikely to be adopted into routine clinical practice around early detection.

Once a cancer has been detected, technology allows much more accurate assessment of the tumour burden and the stage of the disease. This information allows for precise planning of interventions, such as surgery or targeted radiotherapy. Unfortunately, while many cancers detected today are harmless, many others are quite widespread at the time of diagnosis, and the search continues for treatments that can target and eliminate the cancer cells throughout the body. Chemotherapeutic agents have conventionally been used in this situation. The development of chemotherapy was quite slow during the first part of the 20th century, but remarkable responses were obtained with certain tumours, such as choriocarcinoma and seminoma.

Traditional chemotherapy uses chemicals that target rapidly dividing cells, the typical characteristic of cancer. These agents have generally been discovered and developed by trial and error, and as their actions are not specific for cancer cells, their use is associated with significant side effects and toxicity. Many older chemotherapeutic agents are still in daily use and retain efficacy against a number of solid tumours and leukaemias. Dosing regimes and measures to

reduce toxicity have allowed more efficient use of these drugs. Tumours behave not unlike bacteria and, having been exposed to a lethal agent, can develop resistance to its mechanism of action. In addressing the systemic treatment of cancer, researchers have looked at the characteristics of cancer cells and worked to develop agents that will interrupt or turn off specific processes unique to tumour cells.

Progress in understanding tumour biology

In order to understand the newer targeted approaches to cancer treatment, one must have an appreciation of tumour biology.

Normal cell growth and division is highly regulated. Many signalling molecules, including factors that both promote and inhibit growth, are present. These molecules bind to receptors on the cell surface, which then activate intracellular pathways that determine the control of cell processes. Cell growth and division is determined by the balance between stimulatory and inhibitory pathways.

Normal cells die after a certain time, particularly if there is some abnormality within, in a programmed process called apoptosis. Apoptosis can be initiated through activation of cell surface receptors or through intracellular mechanisms. Cancer cells, however, have mechanisms to resist apoptosis. These include interference with surveillance and overproduction of anti-apoptotic proteins. These are potential targets for agents that block the anti-apoptotic cellular mechanisms, and indeed even promote apoptosis, particularly in cells that have been partially damaged by radiation or chemotherapy.

By nature, cancer cells replicate unchecked. They may activate or overexpress growth receptors to compensate for low levels of growth factors. In some tumours, dysfunctional receptors stay activated, encouraging uncontrolled growth. Mutations may keep cells from receiving or transmitting signals that should tell them to stop growing. Such pathways are potential targets for anti-cancer drugs. These drugs may interact with the surface receptors, preventing their activation by growth factors, or may interfere with the intercellular pathways, which will promote uncontrolled growth and replication.

In order for tumours to grow, they need a blood supply. Cancer cells are able to release factors that promote the development of blood vessels and also release chemicals that clear the path for the developing new blood supply. Here is another potential target for intervention; stopping the development of the new blood vessel will predictably inhibit further growth.

Cancer cells are abnormal and are therefore targets for immune response mechanisms. The fact that they originate from host tissue does, of course, complicate the immune response. Cancer cells avoid destruction by immune mechanisms in a number of ways. Inactivating these protective mechanisms can make the cancer cells vulnerable to destruction by the host's immune system. This field, too, has had major advances; so-called checkpoint inhibitors are perhaps one of the most exciting developments.

Many other interventions are under investigation. The point of this discussion is to emphasise the complexity of both the growth and development of cancer cells and the potential targets for interfering with these processes.

New cancer treatments

The new generation of anti-cancer treatments started toward the end of the last century. Some but not all have had dramatic effects on cancers.⁴ For example, in treating Chronic Myeloid Leukaemia (CML), the drug imatinib has changed this disease from a uniformly fatal to a chronic condition with long-term survival.⁵

These new cancer treatments, however, come at a significant financial cost. In determining the cost of medication, one can use the principle of *justum pretium*, or "just price" versus "free market price".⁶ It would seem reasonable that the just price principle should be applied to life-saving medications and interventions and the free market price reserved for luxuries. When imatinib was introduced in 2001, it cost USD 25,000 per patient per year. This price was based on comparison with interferon, which was the accepted treatment for CML at the time. The predicted time for recoupment of development costs at this price was calculated at two years. The effect of the drug is to prolong survival and the numbers

of patients treated with it increased progressively. The price in 2013 hit USD 92,000 per patient per year, raising the question whether the profit gained is excessive.

New cancer treatments are commonly priced similarly or slightly above existing ones. This practice has meant progressive price hikes to the point where most of the newer drugs that hold promise cost around USD 100,000. This prompted a group of haematology and oncology specialists to write the pharmaceutical industry an open letter openly questioning the cost of imatinib, and pointing out price variations by region.⁷

The cost of anti-cancer therapy has come under the spotlight on numerous occasions, as these costs place severe stress on health budgets. Funding authorities are forced to look carefully at data to decide whether any potential improvement in outcomes is cost-effective. The ethics of excessive profit-taking in the situation has to be questioned.

Outlook for cancer treatment

The reality is that the most common cause of death in developed countries is now cancer. With the advances in the understanding of tumour biology and the increasing sophistication of the targeted chemotherapy and immunotherapy agents, improvements in outcomes are occurring rapidly. The U.S. Food and Drug Administration (FDA) approved 18 new cancer drugs in 2015 compared to only six in 2010. It is estimated that 800 ongoing clinical trials for new cancer drugs are currently underway.

The question remains: Can we afford these medications? Can we afford to live longer?

Endnotes

- 1 Brenner, M.H., Commentary: Economic growth is the basis of mortality rate decline in the 20th century — experience of the United States 1901-2000. *International Journal of Epidemiology*, 2005. 34(6): p. 1214-1221.
- 2 Ibid.
- 3 Welch, H.G., et al., Breast-Cancer Tumor Size, Overdiagnosis, and Mammography Screening Effectiveness. *New England Journal of Medicine*, 2016. 375(15): p. 1438-1447.
- 4 Tannock, I.F. and J.A. Hickman, Limits to Personalized Cancer Medicine. *New England Journal of Medicine*, 2016. 375(13): p. 1289-1294.
- 5 Longo, D.L., Imatinib Changed Everything. *New England Journal of Medicine*, 2017. 376(10): p. 982-983.
- 6 Abboud, C., et al., The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts. *Blood*, 2013. 121(22): p. 4439-4442.
- 7 Ibid.

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