

Cancer care burden: aiming at the Achilles heel

S. Ahmed MD,*†‡ R.K Shahid MD,†‡ and K. Gesy MPharm[§]

INTRODUCTION

Cancer is the one of the major causes of death worldwide. More than 16 million new cancer cases are expected by 2020, and it is estimated that cancer will then be the cause of more than 10 million deaths per year¹.

Cancer has become the leading cause of death in Canada. According to the Canadian Cancer Society, 40% of men and 45% of women are expected to develop cancer during their lifetime². With recent advances in cancer management and research, the outcomes of cancer patients—specifically in developed countries—have improved. However, since the early 2000s, the cost of cancer care has exponentially gone up.

Cancer care encompasses a wide range of costs—including financial, social, and psychological burdens—that are difficult to estimate. The worldwide cost of cancer attributable to premature death and disability (not including direct medical costs) has been estimated to be US\$895 billion³. Mounting rates of new cancers, drugs used in cancer care, high-cost innovations and technologies, overutilization of care and futile disease-directed care, and financial hardship for the patients and families are equally contributing to the cancer care burden.

More Cancers, More Expenditure

Cancer incidence rises as the population ages. Ironically, total spending on cancer care is driven mostly by secondary and tertiary care (the cost to treat individual patients); little attention has been paid to primary prevention at the population level.

Novel Cancer Drugs and High-Cost Innovations

The cost of health care has been driven by innovations in medicine. Novel drugs and innovative therapies, new approaches to early detection and staging, new surgical devices, new methods to deliver radiation treatments, and new technologies for diagnosis and surveillance have contributed to rising cancer costs. For instance, the drugs associated with cancer care are estimated to cost approximately US\$40 billion per year globally⁴. In Europe between 1993 and 2004, total sales for cancer drugs alone increased from \$40 million to \$6.2 billion³. The Canadian Cancer Society estimates that cancer drugs cost an average of CA\$65,000 annually per patient. About 1 in 12 patients is not adequately covered to fund that cost⁵. Currently, more than 100 new molecules are in phase III trials. Most new

molecules are priced at CA\$4,000 per month or more (Table 1). Likewise, imaging costs for computed tomography, positron-emission tomography, and magnetic resonance imaging are increasing twice as fast as the overall cost of cancer care.

Overutilization and Professional Services

Specialists influence the greatest proportion of cancer care costs, through use and choice of drugs, types of supportive care, frequency of imaging, and number and extent of hospitalizations^{6,7}. Overutilization is driven by false expectations, non-evidence-informed practice, defensive medicine, financial incentives, off-label use of cancer medicines, and impetus of ability to do everything⁷⁻⁹. For example, routine surveillance testing with serum tumour markers and imaging in asymptomatic patients have not been shown to have clinical value for most solid cancers, but are commonly performed¹⁰. False-positive tests can lead to harm through unnecessary invasive procedures, overtreatment, unnecessary radiation exposure, and misdiagnosis. Likewise, the American Society of Clinical Oncology guidelines recommend the use of white cell-stimulating factors when the risk of febrile neutropenia secondary to a recommended chemotherapy regimen is approximately 20% and equally effective treatment programs that do not require white cell-stimulating factors are unavailable. And yet, the appropriate use of granulocyte colony-stimulating factors for the primary prophylaxis of febrile neutropenia still varies widely in clinical practice^{7,11}. Furthermore, consumer demand and willingness to accept and pay for interventions with marginal benefits also play a causal role in overutilization of cancer care.

Futile Disease-Directed Care

Evidence suggests considerable expenditure for cancer care in the last weeks of life¹²⁻¹⁴. Estimates suggest that at least 20% of patients with solid tumours are receiving chemotherapy within 2 weeks of death¹⁴. Patients and their families can have false expectations despite receiving information on prognosis¹⁵. Overly aggressive cancer treatment near the end of life results in high rates of emergency room visits, hospitalization, or stays in the intensive care unit in parallel with delay in referral to palliative care.

Financial Hardship for Patients and Families

In conjunction with rising cancer costs, people living with cancer are facing a significant financial burden.

TABLE 1 Comparative costs of targeted therapy in Canada for various cancers

Drug	Target	Health Canada–approved indications	Monthly per-cycle cost (CA\$)
Ipilimumab	CTLA4	Advanced melanoma	27,840 (per dose)
Dasatinib	Bcr–Abl	Chronic myelogenous leukemia	4,450
Sorafenib	Multikinase	Advanced hepatocellular cancer	5,521
Cetuximab	EGFR	Advanced head-and-neck cancer	14,232 ^a
		Advanced colorectal cancer	6,620
Crizotinib	Alk1	Advanced lung cancer	8,904
Vemurafenib	B-Raf	Advanced melanoma	5,585
Lenalidomide	IMD	Myelodysplastic syndrome	10,830
		Multiple myeloma	8940
Sunitinib	Multikinase	Advanced renal cell cancer and GIST	4,750
Trastuzumab	HER2	Early-stage and advanced breast cancer	4,254
Pertuzumab	HER2	Advanced breast cancer	4,765
TDM-1	HER2	Advanced breast cancer	7,680

^a One course of treatment with radiation. Prices are based on labelled dosing for an average adult at the Canadian selling price; retail drug costs could be higher.

CTLA4 = cytotoxic T lymphocyte–associated protein 4; EGFR = epidermal growth factor receptor; IMD = immunomodulating drug; GIST = gastrointestinal stromal tumour; HER2 = human epidermal growth factor receptor 2.

Lost wages are a major contributor to the financial hardship experienced by cancer patients and their families. A Canadian study revealed that 91% of households suffer a loss of income or a rise in expenses as a direct result of a cancer diagnosis^{16,17}. Medical appointments are very often uncoordinated and time-consuming, and hence it becomes impossible to hold a job. Inability to work during treatment or while caring for a loved one can result in a dramatic decline in family income. Furthermore, 1 in 5 Canadians have no private supplemental health insurance, and about 20%–30% of Canadians rely solely on government benefit programs or have no coverage at all¹⁸. However, government assistance might be unavailable until nearly all personal savings have been depleted. Gaps and inconsistencies in coverage and services can leave individuals responsible for tens of thousands of dollars in additional costs.

INTERVENTIONS TO ADDRESS THE CANCER CARE BURDEN

Cancer treatment is complex, often involving a variety of services, health care professionals, and settings. Hence, a combination of top-down and bottom-up approaches at various levels is required to overturn the rise in cancer care costs. We propose a framework to harness those cost. Its components include value-based care, behavioral approaches, innovative research and transformed policies, and a focus on the root causes of cancer (Figure 1).

Value-Based Care

Value-based care involves a comprehensive assessment of the outcomes and costs of care and a comparison with other approaches and modalities. Responsiveness to value-based care is increasing, as is the development of new price–value models promoting drugs and technologies

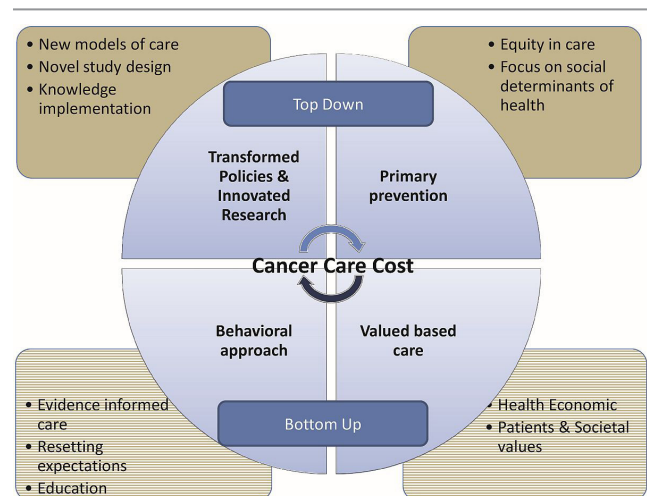


FIGURE 1 Proposed framework to reduce cancer care costs in the short and long term. The cost of cancer care has risen exponentially, with the major contributing factors being the mounting rates of new cancers, the escalating prices of novel cancer therapies, the emergence of high-cost innovations and technologies, and overutilization and futile disease-directed care. A combination of top-down and bottom-up approaches involving value-based and evidence-informed care, shared decision-making, innovative research, transformed policies, and a focus on environmental and social determinants of health are required to overturn the rising costs.

that would substantially improve outcomes but discourage the expansion of marginally effective treatment. Cost-effectiveness is typically evaluated using an incremental cost-effectiveness ratio that compares the experimental treatment with the standard treatment. Usually, the incremental cost-effectiveness ratio is expressed as an incremental cost per life-year gained. The optimal threshold

for cost-effectiveness is not known. In many developed countries, \$130,000 or less is considered an appropriate price at which to buy excellent care for an extra year of life¹⁹.

Little correlation is evident between the actual efficacy of a new drug and its price as measured by cost–efficacy ratios^{9,20–22}. For example, in advanced pancreatic cancer, erlotinib has demonstrated a 0.33-month median improvement in survival at an estimated incremental cost of about \$500,000 per life-year gained. Despite that limited clinical benefit, erlotinib is endorsed by Health Canada and the professional societies²³. Fojo and Grady²² estimated that 18 weeks of cetuximab treatment for non-small-cell lung cancer, which was found to extend life by 1.2 months, costs an average of \$80,000, which translates into an expense of \$800,000 to prolong the life of a patient by 1 year.

Although industry-sponsored estimates place the average cost of research to bring a drug to market at \$1.3 billion, Light and Kantarjian²⁰ showed that such estimates are substantially inflated. Re-evaluation of the methodologic basis of economic decision-making in cancer care—particularly the systematic determination of patient values and what constitutes meaningful benefit—are essential for successful implementation of the value-based approach. Notably, that model of care is more applicable in the setting of incurable than in early-stage cancer. For instance, a new drug in an adjuvant setting that prevents recurrence of cancer and saves a life thereby eliminates the cost of treating advanced disease in the future.

To effectively implement the value-based model, researchers and professional societies have the responsibility to seek better results and to stop endorsing treatments with marginal benefit. Seizing that responsibility will ease the pressure on oncologists when they discuss treatment options. Furthermore, empowering patients through education and shared decision-making, and promoting public education about the evaluation and validation of cancer technologies and the idea that value-based care is not synonymous with poor care can potentially improve care and lower costs. In Canada, the Pan-Canadian Oncology Drug Review and the Pan-Canadian Pharmaceutical Alliance are early steps to guide provinces and territories in making informed drug funding decisions and to promote equal access to cancer drugs across Canada.

Evidence-Informed Care: Behavioral Approach

Physician education is informed by evidence-based medicine. Poor-quality care is described as practices of known effectiveness being underused, practices of known ineffectiveness being overused, and services of equivocal effectiveness being used in accordance with provider rather than patient preference¹³.

Cancer specialists are obligated to provide evidence-based care that is cost-effective so as to minimize waste and eliminate insufficiency. These key recommendations^{6,8,9,24}, in concert with oncologist attitudes and practice, can bring down the cost of cancer care:

- Using shared decision-making and patient engagement during various phases of care
- Using lower-priced options, if available

- Selecting treatment schedules that minimize travel time or time away from work
- Limiting disease-directed therapy on the basis of performance status
- Discontinuing investigations for staging and surveillance that are not evidence-based
- Limiting use of growth factors
- Integrating palliative care into oncology care early

Improving education for health-care professionals with respect to the use of marginally effective or futile treatment is a component that can bend the cancer cost curve. Tools are available to help reset expectations and to assist patients, families, and providers to accept the transition from active treatment to supportive care^{25,26}. Nonetheless, the best method of educating health care professionals and patients to be cost-conscious is a challenge and remains to be investigated. Integration of cost-effectiveness knowledge into the medical oncology curriculum and continuing medical education is a relatively simple task that could positively affect health costs. Physician education could be linked to their Maintenance of Certification program. For instance, using various quality indicators to assess practice in relation to the Maintenance of Certification program is an important means of identifying weakness in practice and addressing the practice gap.

Transformed Policies and Innovative Research

A successful behavioral approach is linked with good policies. Major changes in cancer policies at various levels are required for cancer control and improved access to affordable care while new models of care are applied to control costs by integrating an informed regulatory system, value-based pricing of cancer therapies, compensation for cognitive services, reduction in regulatory bureaucracy on cancer research, and better access to supportive care and home hospice.

New approaches to reimbursement for cognitive services—such as discussing participation in a clinical trial or advanced medical directives, and managing unrealistic expectations in family conferences—are essential. In many cases, cancer care involves uncoordinated sequential visits to multiple providers, departments, and specialties. Minimization of fragmented care and a move to integrated practice units that encompass all the skills and services required for the cancer journey are both needed. Health outcomes measurement should become an integral part of every provider's practice. To eliminate bias against patients with complex needs, outcomes must be adjusted for initial conditions when patients present to the provider²⁷. Moreover, healthy public policy that creates supportive environments, strengthens community action, develops personal skills, and refocuses health services is essential to promote healthy living and to reduce the burden of cancer.

Furthermore, integration of economic and cost-effective health research with novel designs using multi-level frameworks (phase 0, iv, and adaptive trials; complex multimodal clinical trials), prognostic and predictive biomarker studies, quality monitoring programs, assessment of value-based models using real-world patients,

and accounting for indirect costs and effect on family are vital to harnessing cancer care costs. Many early-phase trials do not produce information of the quality needed for a confirmatory phase III trial. Improved clinical trial designs will help to make the clinical trial enterprise more efficient, primarily by earlier detection of inadequate benefit. For example, adaptive designs use interim data to modify an ongoing trial without undermining its validity and integrity, or introducing bias. Bayesian approaches allow for continual reassessment of trial findings. A point-of-care approach involving basic research scientists and clinicians would hasten adoption of treatment improvements and allow researchers to leverage the resources of the clinical service. Furthermore, innovative future clinical study designs based on molecular tumour signatures across multiple tumour sites ("histology-independent trials") will accelerate drug development and reduce costs and duplication.

Primary Prevention: Aiming at the Achilles Heel

Although most cancer results from a complex interaction of genetic susceptibility and environmental factors, a major proportion of malignant diseases is known to be preventable²⁸. It has been estimated that more than 30% of cancer deaths could be prevented by modifying or avoiding key risk factors, including tobacco, obesity, unhealthy diet, lack of physical activity, alcohol use, infection with viral hepatitis and human papillomavirus, and air pollution. Many risk factors add to the cost of other chronic diseases. For instance, recent estimates indicate that tobacco-related illness costs Canadians CA\$4.4 billion in direct health care costs, with an estimated social cost of CA\$17 billion per year²⁹. Differential exposure to modifiable determinants can result in differential rates of cancer incidence and mortality³⁰. Notably, health gradients can be related to poverty, rural or remote location, and language and cultural barriers in various high-risk populations, including socio-economically disadvantaged people, rural residents, and aboriginal, ethnic minority, and immigrant groups. Consequently, a broad vision with a focus on the environmental and social determinants of health, changes in inequitable resource distribution, and dedicated and coordinated efforts informed by principles of equity, collaboration, participation, and capacity-building are prerequisite for reducing the growing cancer burden and, consequently, the uncontrolled costs of cancer care.

Primary prevention care is fragmented and often ineffective and inefficient. Reorganization of prevention, wellness, and routine health maintenance services with sustained funding and a workforce reimbursed for preventive care, the establishment of wellness programs in various sectors, and health promotion are long-term investments in tackling the burden of cancer and other chronic diseases. A comprehensive global tobacco control policy would be an effective and simple way to protect future generations from the rising cancer burden.

The foundation for lifelong good health is set in childhood. Hence, a life-course approach that addresses factors influencing behavior and choices relating to balanced diets and physical activity is vital in tackling the cancer burden. Efforts in primary prevention can be further amplified by

using effective screening programs for early detection of cancers at their most treatable stage.

ACKNOWLEDGMENTS

The authors thank Drs. Anthony Fields and Anne Leis for comments.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare that we have none.

AUTHOR AFFILIATIONS

*Department of Oncology, Saskatchewan Cancer Agency, University of Saskatchewan, Saskatoon, SK; † Department of Medicine, University of Saskatchewan, Saskatoon, SK; ‡ Department of Community Health and Epidemiology, University of Saskatchewan, Saskatoon, SK; § Department of Pharmacy, Saskatchewan Cancer Agency, University of Saskatchewan, Saskatoon, SK.

REFERENCES

1. The global and regional burden of cancer. In: Stewart BW, Wild CP, eds. *World Cancer Report 2014*. Lyon, France: IARC Press; 2015: 16–24.
2. Canadian Cancer Society's Advisory Committee on Cancer Statistics. *Canadian Cancer Statistics 2014*. Toronto, ON: Canadian Cancer Society; 2014. [Available online at: <http://www.cancer.ca/~media/cancer.ca/CW/cancer%20information/cancer%20101/Canadian%20cancer%20statistics/Canadian-Cancer-Statistics-2014-EN.pdf>; cited 6 April 2015]
3. Sullivan R, Peppercorn J, Sikora K, *et al.* Delivering affordable cancer care in high-income countries. *Lancet Oncol* 2011;12:933–80.
4. Hillner BE, Smith TJ. Efficacy does not necessarily translate to cost effectiveness: a case study in the challenges associated with 21st-century cancer drug pricing. *J Clin Oncol* 2009;27:2111–13.
5. Canadian Cancer Society. *Cancer Drug Access for Canadians*. Toronto, ON: Canadian Cancer Society; 2009. [Available online at: http://www.colorectal-cancer.ca/IMG/pdf/cancer_drug_access_report_en.pdf; cited 1 November 2014]
6. Shih YT, Ganz PA, Aberle D, *et al.* Delivering high-quality and affordable care throughout the cancer care continuum. *J Clin Oncol* 2013;31:4151–7.
7. Schnipper LE, Smith TJ, Raghavan D, *et al.* American Society of Clinical Oncology identifies five key opportunities to improve care and reduce costs: the top five list for oncology. *J Clin Oncol* 2012;30:1715–24.
8. Smith TJ, Hillner BE. Bending the cost curve in cancer care. *N Engl J Med* 2011;364:2060–5.
9. Meropol NJ, Schrag D, Smith TJ, *et al.* on behalf of the American Society of Clinical Oncology. American Society of Clinical Oncology guidance statement: the cost of cancer care. *J Clin Oncol* 2009;27:3868–74.
10. Khatcheressian JL, Wolff AC, Smith TJ, *et al.* on behalf of the American Society of Clinical Oncology. American Society of Clinical Oncology 2006 update of the breast cancer follow-up and management guideline in the adjuvant setting. *J Clin Oncol* 2006;24:5091–7.
11. Potosky AL, Malin JL, Kim B, *et al.* Use of colony stimulating factors with chemotherapy: opportunities for cost savings and improved outcomes. *J Natl Cancer Inst* 2011;103:979–82.
12. Earle CC, Neville BA, Landrum MB, Ayanian JZ, Block SD, Weeks JC. Trends in the aggressiveness of cancer care near the end of life. *J Clin Oncol* 2004;22:315–21.
13. Earle CC, Landrum MB, Souza JM, Neville BA, Weeks JC, Ayanian JZ. Aggressiveness of cancer care near the end of life: is it a quality-of-care issue? *J Clin Oncol* 2008;26:3860–6.

14. Harrington SE, Smith TJ. The role of chemotherapy at the end of life: "When is enough, enough?" *JAMA* 2008;299:2667–78.
15. Mackillop WJ, Stewart WE, Ginsburg AD, Stewart SS. Cancer patients' perceptions of their disease and its treatment. *Br J Cancer* 1988;58:355–8.
16. *Five-Year Action Plan to Address the Financial Hardship of Cancer in Canada: A Call for Action*. Toronto, ON: Canadian Cancer Action Network; and Winnipeg, MB: Canadian Cancer Society; n.d. [Available online at: <http://www.cancer.ca/~media/cancer.ca/MB/get%20involved/take%20action/financial%20hardship%20of%20cancer%20in%20canada/financialhardshipofcancer-MB-EN.pdf>; cited 2 November 2014]
17. Hopkins RB, Goeree R, Longo CJ. Estimating the national wage loss from cancer in Canada. *Curr Oncol* 2010;17:40–9.
18. Miedema B, Easley J, Fortin P, Hamilton R, Mathews M. The economic impact on families when a child is diagnosed with cancer. *Curr Oncol* 2008;15:173–8.
19. Kantarjian HM, Fojo T, Mathisen M, Zwelling LA. Cancer drugs in the United States: *justum pretium*—the just price. *J Clin Oncol* 2013;31:3600–4.
20. Light DW, Kantarjian H. Market spiral pricing of cancer drugs. *Cancer* 2013;119:3900–2.
21. Light DW, Warburton RN. Extraordinary claims require extraordinary evidence. *J Health Econ* 2005;24:1030–3.
22. Fojo T, Grady C. How much is life worth: cetuximab, nonsmall cell lung cancer, and the \$440 billion question. *J Natl Cancer Inst* 2009;101:1044–8.
23. Moore MJ, Goldstein D, Hamm J, *et al.* on behalf of the National Cancer Institute of Canada Clinical Trials Group. Erlotinib plus gemcitabine compared with gemcitabine alone in patients with advanced pancreatic cancer: a phase III trial of the National Cancer Institute of Canada Clinical Trials Group. *J Clin Oncol* 2007;25:1960–6.
24. Peppercorn JM, Smith TJ, Helft PR, *et al.* on behalf of the American Society of Clinical Oncology. American Society of Clinical Oncology statement: toward individualized care for patients with advanced cancer. *J Clin Oncol* 2011;29:755–60.
25. Smith TJ, Hillner BE. Concrete options and ideas for increasing value in oncology care: the view from one trench. *Oncologist* 2010;15(suppl 1):65–72.
26. Sepucha KR, Ozanne EM, Partridge AH, Moy B. Is there a role for decision aids in advanced breast cancer? *Med Decis Making* 2009;29:475–82.
27. Porter ME. A strategy for health care reform—toward a value-based system. *N Engl J Med* 2009;361:109–12.
28. Danaei G, Vander Hoorn S, Lopez AD, Murray CJ, Ezzati M on behalf of the Comparative Risk Assessment Collaborating Group (Cancers). Causes of cancer in the world: comparative risk assessment of nine behavioral and environmental risk factors. *Lancet* 2005;366:1784–93.
29. Reid JL, Hammond D, Burkhalter R, Ahmed R. *Tobacco Use in Canada: Patterns and Trends*. Waterloo, ON: Propel Centre for Population Health Impact, University of Waterloo; 2012. [Available online at: http://www.tobaccoreport.ca/2012/TobaccoUseinCanada_2012.pdf; cited 1 July 2014]
30. Ahmed S, Shahid RK. Disparity in cancer care: a Canadian perspective. *Curr Oncol* 2012;19:e376–82.