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Cancer Policy: Pharmaceutical Safety

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Cancer Policy: Pharmaceutical Safety

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Impact of Cost on the Safety of Cancer Pharmaceuticals

1

Karen Fitzner and Frederick Oteng-Mensah

Abstract

Cancer care drug costs are rising due to a variety of factors, and safety concerns account for some of the cost. At the same time, clinical and economic concerns drive drug safety improvements. This chapter examines pressures on drug costs due to the complexity of care and drug therapies, marked structure in which care is provided, and regulatory requirements driving safety.

Keywords

Cancer · Safety · Economics · Cost · Pharmaceutical

1.1 Introduction

1.1.1 Genesis of Thinking About the Impact of Cost on the Safety of Cancer Treatment

Cancer drug costs and safety have garnered considerable attention over the past several years as drug prices rose, and new Food and Drug Administration requirements have been implemented. Drugs such as ipilimumab (Yervoy) are notable for their high price tag of $30,000 per dose while extending life of patients with metastatic melanoma by only 2.1–3.7 months [1]. In early 2011, a news story covered findings of a meta-analysis that examined cancer drug, bevacizumab (Avastin), linking the drug to increased risk for treatment-related death. The story ran shortly after the US Food and Drug Administration (FDA) proposed taking

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action by withdrawing approval of the drug for breast cancer indications [2]. In an earlier example, drug manufacturers agreed to include new box warnings with changed dosage and administration verbiage after four studies showed serious and life-threatening side effects of erythropoiesis-stimulating agents (ESAs) [3].

Unquestionably, prescription drugs for cancer have had a measurable and significant impact on clinical, mortality, and lifestyle outcomes, all of which are directly dependent on drug safety and efficacy. Pharmaceuticals contribute to both considerable benefits for people with cancer but also account for safety concerns and an increasingly large share of treatment cost. The American Cancer Society (ACS) estimates cancer survivorship to have improved from 3 million to 13.7 million within a span of 41 years [4]. While impossible to measure, much of this improvement is due to safety advances. These advances confer notable value in drug safety and efficacy but come at a cost. With the advent of the Medicare prescription drug benefit [5], the US Centers for Medicare and Medicaid Services (CMS) now has a clear stake in drug safety and effectiveness, using its control over coverage and reimbursement to control costs and promote safety.

Telling the cancer drug cost and safety story is akin to the conundrum over the chicken and the egg—which comes first. Poor safety harms patients and increases treatment cost. At the same time, safety advances are likely to be driven by the rising costs of care because societies will demand greater levels of safety as they become richer.

The purpose of this chapter is to inform readers about the economics associated with the interplay between safety, costs of cancer treatment, and outcomes of cancer care. The chapter begins with a general discussion of safety, cost, cancer care expenditures, and processes that aim to ensure drug safety. This information is provided as a backdrop for the more focused discussion of safety and cost of cancer pharmaceuticals that occurs later in the chapter.

1.1.2 Safety Definition

According to the Merriam Webster Dictionary, safety is “freedom from harm or danger: the state of being safe; the state of not being dangerous or harmful” [6]. This definition easily applies to cancer care and drugs. The notion of drug safety is predicated upon the Hippocratic Oath and involves considerable testing and surveillance that occur in two related but separate phases. In the first phase, the drug must demonstrate sufficiently high safety so that it can receive approval by the designated regulatory agency, which in the US is the Food and Drug Administration (FDA) [7, 8]. The second phase is implemented post-approval after the drug is available in the marketplace and being prescribed to patients. Phase two, known as pharmacovigilance (or Drug Safety), is characterized by a due diligence process aimed at preventing adverse effects from the use and treatments with pharmaceutical products.

Pharmacovigilance is formally defined as the pharmacological science relating to the collection, detection, assessment, monitoring, and prevention of adverse effects

with pharmaceutical products [9]. In the US, in addition to the FDA, the US the Agency for Healthcare Research and Quality (AHRQ), Center for Quality and Safety strives to prevent medical errors and promote safety and quality of patient outcome [10]. AHRQ's approach to promoting pharmaceutical quality and safety aims primarily at reducing risk of maltreatment from healthcare delivery by advancing proper care practices to promote greater value to patient health outcomes.

1.1.3 Cost

Total cancer treatment costs are significant and are driven in part by in the current US regulatory, reimbursement, and legal systems, each of which also has the ability to affect the clinical efficacy, safety, and cost of pharmaceuticals. Terminology is, however, tricky. Cost of cancer care and pharmaceuticals typically differs from price, charges, or amount paid. Cost comprises direct medical costs, indirect costs of care, and a temporal aspect.

Economists speak about economic cost, opportunity cost, and marginal cost. Economic cost includes the (1) opportunity cost, which is the full cost of resources spent making one choice over another to achieve the same objective, and (2) accounting cost, which is the amount of money spent carrying out the action. Opportunity costs are incurred when resources are spent to achieve safer drugs—dollars and staff time dedicated to safety could have been used, for example, to build a new patient care room. Marginal cost describes the additional cost of doing one more thing such as treating one more patient or giving one more dose of medication to a patient who is already taking the drug.

1.1.4 Direct Medical Cost

Direct medical cost that accrues from the use of medical resources, such as, physicians, hospitals, insurance, and patient contributions for cancer treatment purposes. Direct medical costs differ for different cancer types and stages of the disease [11, 12] (see Table 1.1). Two main costs are measured here: incidence costs, which refer to costs at diagnosis and/or in the event of a specific episode in a cluster of patients categorized by a specific phase of "clinical characteristics" and

Table 1.1 Cost of cancer prevalence by phase of care

	Cost of cancer care by phase of care			Prevalence by phase of care		
	Initial	Continuing	Last	Initial	Continuing	Last
2010	$40,464	$46,643	$37,459	1,079,991	11,790,829	900,965
2020	$48,317	$61,373	$48,077	1,306,479	15,547,832	1,216,414
Increase (%)	$19.4	31.6	$28.3	21.0	31.9	35.0

Source National Cancer Institute. http://costprojections.cancer.gov

prevalence costs refer to costs incurred on survivors in any given year [12]. The AHRQ estimates that in 2011 the direct medical costs for cancer in the US equaled $88.7 billion [13]. Half of this expenditure covers hospital outpatient or doctor office visits, slightly more than one-third (35%) covered inpatient hospital stays, and 11% was spent on prescription drugs. The National Institutes of Health, National Cancer Institute (NCI), however, reports that the direct medical cost of cancer for all sites was $124.57 billion in 2010 [14]. Table 1.1 includes information provided by the NCI showing both cost and prevalence increases.

1.1.5 Indirect Costs of Cancer

The true cost of cancer care includes patient contributions to insurance payments through copays and deductibles, out-of-pocket costs, and costs associated with time off work and in transit as well as intangible costs such as pain and suffering. These are described as "indirect costs." Indirect medical cost refers to the time value of money lost due to sick days and/or productivity losses from cancer deaths. Indirect medical costs are estimated by putting monetary value to "lost opportunities" employing human capital and willingness-to-pay estimation approaches. There are two types of indirect medical costs: Morbidity costs are for example costs that accrue from lost work due to patients' inability to work, and mortality costs refer to loss of future productivity from premature deaths. Cancer-related losses owing to premature death are estimated at $140.1 billion in 2011.

Indirect costs (also known as indirect morbidity costs) are often ignored when thinking about patient care but are vital to understanding patient adherence to prescribed medications and treatment protocols. Indirect costs are those that the patient bears in seeking and obtaining medical care but are not accounted for in the other measures. These include measurable out-of-pocket costs, transportation expenses, lost work/absenteeism, and intangibles such as suffering and pain. While more difficult to measure than direct medical costs, indirect costs of cancer are estimated to equal $20.9 billion, as per 2011 estimations [14].

1.1.6 Trends in Health Care Spending Dedicated to Cancer in US

This section considers underlying cancer cost trend factors that caught the attention of CMS and other payors who have sought cost containment strategies including risk management to mitigate issues arising from poor safety.

Cancer care is costly overall, accounting for roughly 5% of the US's expenditure on health, which currently approximates to 17.1% of GDP [15, 16]. The National Institutes of Health (NIH) estimated the total burden of cancer care cost for 2011 as $263.8 billion [17]. This figure is likely to increase as advances in cancer medical care technology and pharmaceuticals prolong survivorship from the disease, thereby improving the lives of cancer patients. Researchers from the National

Table 1.2 Estimated national cancer expenditures in 2010 and 2020 under different incidence and survival trend assumptions

Cost in US 2010 billion dollars								
	2010	Assumption for 2020 projection						
						Trend incidence and survival scenario and cost increase		
	Base	Base	Trend incidence	Trend survival	Trend incidence and survival	2% overall	2% in initial and last year phase cost	5% in initial and last year phase cost
Breast	$16.50	$20.50	$18.91	$20.69	$19.08	$23.24	$21.37	$25.64
Colorectal	$14.14	$17.41	$14.35	$17.83	$14.70	$17.67	$16.68	$20.39
Lung	$12.12	$14.73	$12.14	$15.23	$12.53	$15.19	$14.73	$18.84
Lymphoma	$12.14	$15.26	$15.00	$15.71	$15.44	$18.66	$17.27	$20.69
Prostate	$11.85	$16.34	$15.32	$16.43	$15.41	$18.53	$16.67	$19.02
Leukemia	$5.44	$6.95	$6.66	$7.24	$6.94	$8.38	$7.78	$9.35
Ovary	$5.12	$6.03	$4.49	$6.27	$4.64	$5.64	$5.26	$6.42
Brain	$4.47	$5.53	$5.38	$5.79	$5.62	$6.82	$6.51	$8.18
Bladder	$3.98	$4.91	$4.41	$4.98	$4.47	$5.38	$4.90	$5.71
Kidney	$3.80	$5.12	$6.07	$5.30	$6.29	$7.56	$6.99	$8.30
Head/Neck	$3.64	$4.34	$3.79	$4.40	$3.84	$4.65	$4.40	$5.46
Uterus	$2.62	$3.05	$2.84	$3.04	$2.83	$3.42	$3.24	$4.00
Melanoma	$2.36	$3.16	$3.76	$3.18	$3.78	$4.60	$4.06	$4.58
Pancreas	$2.27	$2.83	$2.81	$3.16	$3.13	$3.80	$3.75	$4.92
Stomach	$1.82	$2.26	$1.81	$2.40	$1.92	$2.31	$2.25	$2.88
Cervix	$1.55	$1.54	$1.20	$1.55	$1.21	$1.46	$1.39	$1.73
Esophagus	$1.33	$1.76	$1.70	$2.04	$1.97	$2.38	$2.32	$2.97
All sites	$124.57	$157.77	$147.57	$165.21	$154.70	$186.69	$172.77	$206.59

Source National Cancer Institute. Table 4: Estimates of the national expenditures for cancer care in 2010 and 2020 in 2010 billion dollars under different assumptions of cancer incidence and survival trends. http://costprojections.cancer.gov/expenditures.html#f1

Cancer Institute (NCI) an affiliate of US National Institutes of Health (NIH) postulate that cancer care expenditures could reach $158 billion dollars representing 27% increase over 2010 estimated figures [18]. However, cancer largely attacks older populations and with the aging baby boomers, the incidence and cost numbers are likely to be as much as $207 billion, as shown in Table 1.2.

Better knowledge and understanding of the mechanisms underlying cancer account for some of the cost of care and help to drive safety and patient outcome improvements. Advances in pharmaceutical technology now show that cancer is not a single disease but multiple of hundreds of distinctive diseases. Researchers are using this knowledge to increase survival rates and gain additional years of life for affected patients. This is reflected in a 20% reduction in all cancer deaths in the United States from 1990 figures. These advances, however, come at a cost; PhRMA companies over a period of 14 years invested in excess of $550 billion in new drug

development and regimen, of which $51.1 billion was spent in 2013 alone [19]. Notwithstanding these advances, cancer is the second leading cause of deaths in the United States. The American Cancer Society (ACS) in 2014 estimated that 1.6 million people will be diagnosed with cancer and approximately 600,000 will die from the disease, about 1600 people in a single day [20].

1.1.7 United States Cost of Cancer Pharmaceuticals

Certainly, cancer drug cost increases since 2005 correlate with higher quality, increased safety, and decreased mortality. Table 1.3 presents the direct, indirect, and overall cost of cancer pharmaceuticals from 2005–2015. Drugs such as Imatinib (Gleevec), available since 2001, treat acute lymphoblastic leukemia, chronic myeloid leukemia, and gastrointestinal stromal tumors with considerable success rates. The annual costs of these therapies are, however, significant and growing. The price for Gleevec, for example, was around $30,000/year in 2001, but by 2012, the price rose to more than $90,000/year [21]. High prices are also associated with many recently approved drugs that are deemed safe, such as immunotherapy ipilimumab, which helps train the immune system to recognize and attack cancer cells and extend life. The implied cost outlays are rising and substantial which also impacts the economic, financial, and patient health safety.

Table 1.3 US cost of cancer pharmaceuticals

Fact year	Data year	Direct cost ($ billion)	Indirect cost		Overall cost ($ billion)
			Morbidity cost ($ billion)	Mortality cost ($ billion)	
2005	2004	69.4	16.9	103.5	189.8
2006	2005	74.0	17.5	118.4	209.9
2007	2006	78.2	17.9	110.2	206.3
2008	2007	89.0	18.2	112.0	219.2
2009	2008	93.2	18.8	116.1	228.1
2010[a]	2010	*102.8*	*20.9*	*140.1*	*263.8*
2011[a]	2010	102.8	20.9	140.1	263.8
2012[b]	2007	103.8	–	123.0	226.8
2013[b]	2008	77.4	–	124.0	201.5
2014[b]	2009	86.6	–	130.0	216.6
2015[b]	2011	88.7	–	–	–

Source Compiled from American Cancer Society Cancer Fact and Figures 2005–2015
[a]Fact year publications for 2010 and 2011 both reported similar data
[b]The estimates are made from a different data source: the Medical Expenditure Panel Survey (MEPS) from the AHRQ, it is therefore not comparable with fact year data from 2005–2011 (American Cancer Society)

1.1.8 Types of Concerns Relating to Cancer Therapy (Pharmaceuticals) and Safety

The Food and Drugs Board (FDA) approved drugs for the market mainly based on safety and effectiveness from clinical trials but not necessarily on efficiency. Therefore, it has been failing its way in investigating how costs of cancer pharmaceuticals impact the safety of patients. It is contended that the rate of growth of costs for cancer pharmaceuticals is increasing at an unsustainable rate and if left unchecked could lead to dire consequences on the safety of cancer patients. Unsustainable costs are sure to impact patient safety negatively as patients may skip pertinent therapeutic treatments due to high out-of-pocket and co-payments or suffer insolvency issues after paying for such procedures even with the help of insurance [22–24].

According to Hall (2013), the NCI estimated 1.7 million new Americans were to suffer from various forms of cancer with 580,000 of new and old cases dying from cancer-related causes in 2013. The dismal aspect of the impact of costs on safety is that some FDA-approved cancer drugs have "minor survival benefits, if any" [25]. Although drugs such as ipilimumab have the capability of extending life by a few months and reducing sizes of malignancies, they hardly can cure common forms of cancers. These gains often come at astronomical prices [26], which drive cost containment and risk management initiatives.

Safety-related costs are reflected in clinical, regulatory, and financial responses to gaps in drug safety and increase the burden on multiple stakeholders. Concerns relating to safety range from high prices with very low marginal outcome effect on patient safety [27, 28, 29]. There are also concerns about effective and potent drugs that have the capability of extending life with such huge financial outlays that it toxically impacts the economic and financial life of survivors and to healthcare market failure due to excessive regulations [30, 31]. In all these forms, the underlying premise is that the costs of some cancer pharmaceuticals may outweigh their value or "clinical benefits."

High costs are reflected in clinical, regulatory, and financial responses to gaps in drug safety and increase the burden on multiple stakeholders. This is exacerbated by the inclination of both physicians and patients to try out any regimen even if it has a limited purported advantage of buying additional hours or days of life. Such practices have the tendency of creeping into moral hazard[1] issues, giving rise to overutilization of resources, hence the huge cancer care costs [32].

[1]Moral hazard is a situation in which one party gets involved in a risky event knowing that it is protected against the risk and the other party will incur the cost. It arises when both the parties have incomplete information about each other. Source: http://economictimes.indiatimes.com/definition/moral-hazard.