

# Advancing Comparative Studies of Patterns of Care and Economic Outcomes in Cancer: Challenges and Opportunities

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Cancer is a leading cause of morbidity and mortality worldwide (1). Cancer also accounts for a substantial proportion of health-care expenditures as well as productivity losses due to morbidity and premature death (2). Because incidence increases with age for most cancer sites (3,4), and populations are aging in most developed countries, prevalence is expected to increase appreciably in the future (2,5–8). Additionally, ongoing improvements in early detection and use of effective treatments are associated with improved survival following diagnosis, also increasing cancer prevalence. As a result of these trends, related medical expenditures (6) and costs associated with morbidity (9) and premature mortality (10,11) are expected to be even larger in the future. Moreover, health-care delivery trends, in particular the increasing use of expensive new chemotherapy drugs (12,13), are projected to be associated with increased costs of cancer care in the future. Measuring and projecting the economic burden associated with cancer and identifying effective policies for minimizing its impact are increasingly important issues for health-care policy makers and health-care systems at multiple levels.

Internationally and regionally, there is tremendous diversity in organization and financing of health-care systems, health-care utilization, and cancer care delivery, all of which are associated with variation in cancer outcomes and spending. Selected cancer statistics, measures of health-care services utilization, and overall spending obtained from the Organisation for Economic Co-operation and Development (OECD) (14,15) are listed in Table 1 for several countries with data featured in this monograph. As shown in Table 1, these measures vary significantly by country (14). In 2009, the average cancer mortality rate for women across 34 OECD countries was 124 per 100 000, ranging from 111 per 100 000 in France to 143 per 100 000 in Canada. General health-care utilization, such as the average length of a hospital stay, number of physician visits, or the use of imaging per 1000 individuals, also varies substantially across country. For example, the rate of magnetic resonance imaging (MRI) exams is 97.7 per 1000 individuals in the United States, but 46.3 per 1000 on average across the OECD countries. Other measures such as recent cervical cancer screening range from 39.0% of women aged 20–69 in Italy to 85.9% in the United States, with an average of 61.1% across OECD countries.

Large differences in health-care expenditures, ranging from \$2964 per capita in Italy to \$8233 in the United States (in US dollars, adjusted for purchasing power parity), are also reported. The OECD average per capita spending was \$3265. Within health-care spending, the percentage of public expenditures ranged from 48.2% in the United States to 83.2% in the United Kingdom, with an OECD average of 72.2%. Other components of health-care systems, including coordination of care delivery, administrative costs, negotiation and payment of hospitals, physicians, pharmaceuticals, and input prices, also vary by country and organization of health systems (16).

This diversity in health-care delivery, expenditures, and cancer outcomes suggests that comparative studies between health-care systems and/or countries might inform evaluation, development, or modification of policies related to cancer screening, treatment, and programs of care delivery (eg, hospice care for cancer patients at the end of life). Such comparisons of cancer patient outcomes between different models of health-care delivery can help identify best practices, serve as benchmarking of “high-quality” or “high-value” cancer outcomes and related costs, or be used as contemporary “usual care” comparisons to evaluate the introduction of cancer control interventions. This concept of using cross-national comparisons of health outcomes to identify lessons learned in countries with high-quality outcomes and reduce health disparities elsewhere is highlighted in the recent Institute of Medicine report, *U.S. Health in International Perspective: Shorter Lives, Poorer Health* (17). At the same time, underlying differences in the distribution of population characteristics, cultural attitudes, social and health-care policies, availability of specialists and primary care providers and relative mix of specialty care, physical environments, and data availability make between-health system and between-country comparisons complex (17). As described by Karanikolos et al. in this monograph (18), health systems can influence cancer outcomes through the comprehensiveness of health insurance coverage, the rate at which effective innovative treatments are introduced, and the quality of care as measured by timely and equitable access to diagnostic and specialty care, and coordination of that care.

Some of the observed and measured variation in health outcomes and utilization across countries also reflects differences in types of data sources available and comprehensiveness of

**Table 1.** Cancer incidence and mortality rates and selected health-care delivery and expenditure characteristics by country\*

		United States	United Kingdom	Canada	Italy	France	OECD average for 34 countries
Cancer statistics†	Cancer incidence rates per 100 000 (2008)	300.2	269.4	296.6	274.3	300.4	260.9
	Colorectal cancer, 5-year relative survival rate (2004–2009 or available years)	64.5	53.3	63.4		57.0	59.9‡
	Cancer mortality rates per 100 000 (2009 or nearest year)						
	Females	130	141	143	117	111	124
	Males	185	199	205	212	221	208
Health services utilization (2010 or nearest year)	Average length of hospital stay in days	4.9	7.7	7.7	6.7	5.7	7.1
	Average annual number of physician visits per capita	3.9	5.0	5.5	—	6.9	6.4
	Cervical cancer screening in women aged 20–69, %	85.9§	78.7§	75.3§	39.0	72.4§	61.1¶
	MRI exams per 1000 persons	97.7	40.8	46.7	—	60.2	46.3
	CT exams per 1000 persons	265	76.4	126.9		145.4	123.8
Overall health-care spending# (2010 or nearest year)	Health-care spending per capita	\$8233	\$3433	\$4445	\$2964	\$3974	\$3265
	Out-of-pocket health-care spending per capita	\$970	\$306	\$631	\$528	\$290	\$558
	% public expenditure on health	48.2%	83.2%	71.1%	79.6%	77.0%	72.2%

\* Data from Organisation for Economic Co-operation and Development (OECD) (15). CT = computed tomography; MRI = magnetic resonance imaging.

† Incidence and mortality rates age-standardized.

‡ Colorectal cancer 5-year relative survival based on 16 countries.

§ Cervical cancer screening measured by survey.

|| Cervical cancer screening measured by program data.

¶ Cervical cancer screening measured by OECD average from 17 countries.

# Spending in US dollars adjusted for purchasing power parity.

population coverage for the data source. Cancer incidence is typically collected in geographically defined, population-based cancer registries using consistent definitions, although the degree of registry population coverage varies and can be limited to cities or larger regions, or cover entire countries. Within countries, substantial geographical variation in cancer incidence has been reported, even after controlling for some key population characteristics (19). On the other hand, the cervical cancer screening measures reported by the OECD are based on self-report from household surveys in some countries, but health-care delivery program data in other countries. Self-report has been shown to overstate screening rates compared with medical record data (20), suggesting that the wide range in cervical cancer screening among the selected countries in Table 1 (ie, 39.0%–85.9%) reflects in part the data sources used for the comparison. Thus, variations in the comprehensiveness or the particular characteristics of data sources can also lead to apparent differences in outcomes, utilization, and expenditures.

Variation in data sources is one of many factors complicating comparative studies of cancer outcomes, utilization, and expenditures. For example, international comparisons of 5-year survival rates and costs of care following colorectal cancer diagnosis will also be influenced by the age structure of and risk factor prevalence within the populations, underlying prevalence of screening and distribution of stage of disease at diagnosis, methods of identifying relevant patients (eg, registry, hospital discharges), access to guideline-consistent initial and surveillance care, policies related to coverage of relevant treatment strategies following diagnosis, and competing causes of death. Thus, the complexity of estimating the impact on costs of simultaneous trends in cancer incidence, survival, and patterns of care requires that multidisciplinary approaches be adopted.

In September 2010, the National Cancer Institute, University of Roma Tor Vergata, Istituto Superiore di Sanità, and Institute of Research on Population and Social Policies, National Research Council, co-sponsored a meeting “Combining Epidemiology and Economics for Measurement of Cancer Costs” to discuss interdisciplinary approaches for estimation of the burden of cancer and the feasibility of international and health-care system comparative studies of cancer outcomes (21). That meeting was the basis for initiating this monograph. It contains an overview of key aspects of health-care systems (18), several systematic reviews of published studies of patterns of care and costs associated with cancer (22–24), and a series of comparative papers either between countries (25,26) or between health systems within a country (27,28). The final section begins with an illustration of how simulation modeling can inform cancer care decision making (29). It concludes with a future directions paper that examines the opportunities and challenges associated with improving the scientific quality and usefulness of comparative studies of the burden of cancer and interventions to reduce it (30).

### Systematic Reviews of the Literature Describing Patterns of Cancer Care and Economic Outcomes

Patterns of cancer care are directly related to cancer outcomes and associated costs. In some settings, actual payments or expenditures are not available, and instead, standardized unit costs are applied to service frequency. Thus, an understanding and documentation of patterns of care are a necessary, but not sufficient, first step for understanding the variation in the cost of care and other economic outcomes. This section of the monograph consists of systematic

reviews of the published literature describing treatment patterns and associated economic outcomes, using colorectal cancer as an illustrative example. In addition to providing contemporary information about patient receipt of cancer treatment and associated costs in multiple countries, these reviews offer an overview of relevant data sources and a critical assessment of the completeness of reporting and comparability across studies.

Butler et al. (22) and Chawla et al. (23) conducted companion systematic reviews of published studies of patterns of care following colorectal cancer diagnosis, including initial treatment with surgery, chemotherapy, and radiation therapy; surveillance following initial treatment; and end-of-life care. They abstracted study characteristics, including study country, data sources for identifying cancer patients and health services, study sample size, patient characteristics, type(s) of care measured, and key findings. Importantly, underlying population characteristics, population representativeness, patient and tumor characteristics associated with prognosis (eg, age, stage at diagnosis), data sources, and types of care evaluated and their measurement varied widely both within and across countries. For example, analyses using the ongoing linkage of SEER cancer registry and Medicare claims data (31) in the United States are restricted to Medicare beneficiaries age 65 and older with fee-for-service coverage. Although the majority of newly diagnosed cancer patients are age 65 and older, findings from these SEER-Medicare studies are not necessarily generalizable to the population younger than 65 or to populations in the same age group with other types of health insurance coverage within the United States. Additionally, these studies may not be representative of the entire United States in cross-country comparisons. On the other hand, studies conducted solely in the hospital setting may include all hospitalized patients of all ages, but do not have key information about cancer diagnosis (eg, stage at diagnosis) or may include only inpatient care and not have longitudinal information about ongoing care or vital status. Thus, studies of rectal cancer surgery conducted only in the hospital setting may be incomplete with regard to important trends in the use of neoadjuvant therapy and sphincter-sparing surgery. Importantly, any comparative study based on these data sources will need to be restricted to the subset of patient populations and types of care that can be consistently measured in both data sources. Studies are rarely stratified by these key characteristics, and hence comparisons between published studies are difficult. Further, diversity in health-care systems and health insurance coverage of cancer care makes cross-country comparisons of patterns of care and associated costs all the more challenging.

Yabroff et al. (24) conducted a systematic review of studies of the economic burden associated with colorectal cancer and report *direct medical care costs*, including inpatient care, outpatient or ambulatory services, surgery, chemotherapy and radiation therapy; other *direct non-medical care costs*, such as transportation to and from medical care, time spent by family members providing home care, and patient time; and *productivity or "indirect" costs*, which represent lost or impaired work or leisure time due to morbidity or early death from disease, and are typically measured from the societal or employer perspective. Unlike direct medical costs, which can be measured from health insurance payments or the application of standardized cost or reimbursement rates to

services, direct non-medical costs and indirect costs are not typically measured explicitly. In addition to abstracting and reporting types of costs at the aggregate and per capita levels, they report study country, health-care delivery setting, methods for identifying incident and prevalent colorectal cancer patients, types of medical services included, patient characteristics, and key findings, presented in terms of both incidence-based and prevalence-based estimates. When these myriad study characteristics vary together, as is typically the case, even patterns of care or cost calculations with seemingly the same objective are difficult to compare directly. Moreover, complicating factors such as features of the health-care delivery system, accompanying payer models, and data availability all vary by country.

These three systematic reviews offer recommendations for developing data infrastructure and for standardizing measures and reporting of patient characteristics associated with patterns of care or economic outcomes (eg, stage at diagnosis, comorbidity), with the goal of improving comparability across studies. They also identify areas for improving the comprehensiveness of analyses of patterns of care and the economic burden of cancer, particularly those aspects that are understudied, such as end-of-life care, patient and caregiver time costs, and productivity losses. Ultimately, findings suggest that valid cost comparisons can be developed de novo with explicit standardization of patient populations, types of medical services included, measures of costs, choice of methods, and specification of the context (eg, within- or between-health systems in a country vs cross-country).

## Comparative Studies

As described previously and shown in Table 1, aggregate data can be useful in highlighting differences across countries in health-care delivery, expenditures, and outcomes. Similarly, a recent historical evaluation of cervical cancer screening prevalence and mortality rates in the United States and the Netherlands offers insight into the differential impact of screening frequency, age of initiation and cessation of screening, and insurance coverage policies in the two countries (32). However, a better understanding of the impact of cancer control interventions and associated costs requires individual-level information about patient outcomes and costs in comparable patient populations, with complete information about treatment by stage at diagnosis and other factors that might impact both outcomes and costs. Yet few comparative studies have assessed patterns or costs of cancer care, in part due to absence of standardized data elements measured in the same manner across settings.

This section of the monograph consists of four comparative studies of cancer care across health systems or countries, with the common goals of providing examples and lessons learned that might be applied to other comparative studies, as well as recommendations for future research. One approach is the supplementation of existing data systems using common standards and data quality control measures to allow comparability. EURO-CARE (33,34), a collaborative research project measuring cancer survival in Europe using population-based cancer registry data from more than 20 countries, and the CONCORD program (35), covering population-based cancer registries in more than 30 countries, are prime examples of this approach. These collaborative efforts use

standardized measures for comparability of cancer data to conduct more detailed systematic comparisons of survival following diagnosis for most adult cancers, accounting for underlying population characteristics, such as age structure, competing (ie, noncancer) mortality rates, and race. In this monograph, Gatta et al. use data from EURO CARE-4, supplemented with macroeconomic and health system data from the OECD and the European Observatory on Health Care Systems, to evaluate survival rates for breast, colorectal, and prostate cancer across 19 countries (26). This study uses results from EURO CARE-4 “high-resolution” studies, which include detailed information on stage at diagnosis, staging procedures, and treatment for a sample of cancer patients in each registry. Specifically, they evaluated the association between several summary measures—including total national expenditure on health, investments in health-care infrastructure, and availability of medical devices or equipment—and a classification of the health-care system based on the funding model, adherence to standard cancer care, and 5-year relative survival as an outcome measure. This novel study serves as a model for evaluating macroeconomic measures when assessing differences in cancer outcomes across countries, with the goal of identifying best practices and improving cancer survival throughout Europe. The authors also highlight differences in measures across countries and inconsistencies in population completeness from cancer registries in different countries.

The additional information required for the “high-resolution” studies derived from the EURO CARE project is not routinely collected and requires an additional effort from population-based cancer registries. Similarly, in the United States, the National Cancer Institute and Centers for Disease Control and Prevention conduct cancer registry-based patterns of care studies with more detailed data collection for a sample of newly diagnosed cancer patients about health insurance, characteristics of the hospital where surgery was performed, staging, testing for treatment response (eg, K-RAS), and receipt of adjuvant therapies, including chemotherapy, hormonal therapy, and biological modifiers and immunotherapy (36,37). A related approach to conducting comparative studies across country or health systems capitalizes on existing and sustained linkages of cancer registry and administrative health data (eg, SEER–Medicare), and then study teams work to ensure the consistency of patient populations, services and costs measured, and appropriate methods for evaluation of patient outcomes (38,39). In this monograph, Gigli et al. (25) conducted a comparative study of colorectal cancer care in elderly populations in the United States and Italy. Study teams in both countries had expertise with their respective cancer registry and administrative data, and reimbursement policies. They applied the same selection criteria to identify similar cohorts of newly diagnosed elderly colorectal cancer patients in the linked SEER–Medicare data in the United States and cancer registry data linked to information on hospital discharge cards in two regions in Italy. They identified cancer services with comprehensive information for the cohorts in both countries during the period of the study and compared patterns of colorectal cancer treatment during the first year following diagnosis, including hospitalizations, receipt of surgery, chemotherapy, and radiation therapy. They also compared the timeliness of surgery following

diagnosis and adjuvant therapy following surgery. Although patterns of care within stage at diagnosis were generally similar, they found greater use of adjuvant therapy in the US cohort, a higher percentage of open abdominal surgeries in the Italian cohort (and more use of endoscopic procedures in the US cohort), and more hospital days in the Italian cohort, despite similar numbers of hospitalizations. Additionally, a greater percentage of patients in Italy were diagnosed with advanced disease at diagnosis, suggesting that further evaluation of colorectal cancer screening prevalence, even at the aggregate level, might also be informative. More detailed evaluation of patient outcomes and related costs would also provide more information about the impact of the observed variation in treatment. Finally, in appraising one of the few examples of “head-to-head” comparisons in cancer care between the United States and a European country, where there are many structural differences in health-care delivery and reimbursement, the authors emphasized the importance of ensuring the comparability of populations and the completeness of treatment information.

Fishman et al. (27) also conducted a comparative study with administrative data linked to cancer registries, but within the United States and between fee-for-service and managed care delivery systems. Specifically, they selected an elderly population with newly diagnosed colorectal, prostate, breast, and lung cancers from either SEER–Medicare with fee-for-service coverage, or state-based registry data linked to Medicare Advantage–managed care plans in a subset of the Cancer Research Network (CRN) (40). They report differences, by health-care system, in stage of disease at diagnosis and in inpatient and outpatient care in the 6-month period preceding and 6 months after the cancer diagnosis. Their findings illustrate the importance of differences in the underlying patient characteristics and the mix of inpatient and outpatient care under the two systems. These findings add to the limited research evaluating cancer care in managed care compared with fee-for-service settings in the United States (41,42) and point to the critical importance of comprehensive and comparable data when comparing outcomes across systems. This study also highlights the potential of comparative studies of cancer care and outcomes in evaluating different organizational models of care.

The complications arising in comparative studies of patterns of care are compounded when one tries to assess and contrast cancer care costs in different settings. In addition to structural differences in the organization and financing of health care and systematic variation in patient characteristics and patterns of care, differences in the costs of care across health-care systems also reflect differences in input prices. In the final paper of this section, O’Keeffe-Rosetti et al. (28) describe the development of a standardized relative resource cost algorithm (SRRCA) for comparative studies of the costs of cancer care between different health systems, specifically Medicare fee-for-service and Medicare-managed care in the United States. The SRRCA adapts 15 payment systems used by Medicare to reimburse fee-for-service providers for covered services to health-care utilization data, so that the observed variation in expenditures reflects only variations in the mix and volume of the various medical care services delivered to patients, and not variation in prices in the same inputs.

The SRRCA can be applied in multiple managed care plans and across fee-for-service delivery systems to create consistent relative cost data for economic analyses. These Medicare payment systems are developed separately for short-term stays in general hospitals, inpatient rehabilitation facilities and long-term care hospitals, psychiatric hospitals, physician services, hospital outpatient services, ambulatory surgical centers, laboratory services, skilled nursing facilities, home health services, outpatient dialysis, hospice, ambulance services, durable medical equipment, and pharmacy care. Importantly, the SRRCA can be systematically applied to service use in individuals with and without cancer, allowing for comparison of cancer patients and noncancer control populations across health-care delivery settings, thus informing a wide variety of research questions. Data harmonization issues, more specifically those related to consistency of utilization and resource intensity definitions and measures, will determine how well the SRRCA can be adapted for international comparisons. As highlighted by the authors, a challenging but important task is focusing on differences in utilization, health outcomes, and expenditures across systems and countries to improve the quality of cancer care.

## Policy Applications and Future Directions

The final section of this monograph describes a prostate cancer simulation model from the Cancer Intervention and Surveillance Modeling Network (CISNET) project (43). In this paper, Etzioni et al illustrate how a detailed and calibrated natural history of disease model can be used to inform policy decisions about the harms and benefits of cancer control interventions (29). This section also contains a future directions paper that synthesizes key themes, including the importance of data infrastructure development and standardization of measures and data collection, to promote comparability in analyses of patient populations, cancer diagnosis information, treatment, and components of economic burden (30). Finally, we draw on a wealth of international knowledge and experience in highlighting the utility of comparative studies and in formulating future directions and research priorities.

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