Health Economics Research: Cancer Treatment

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On behalf of the Cancer Treatment Workgroup

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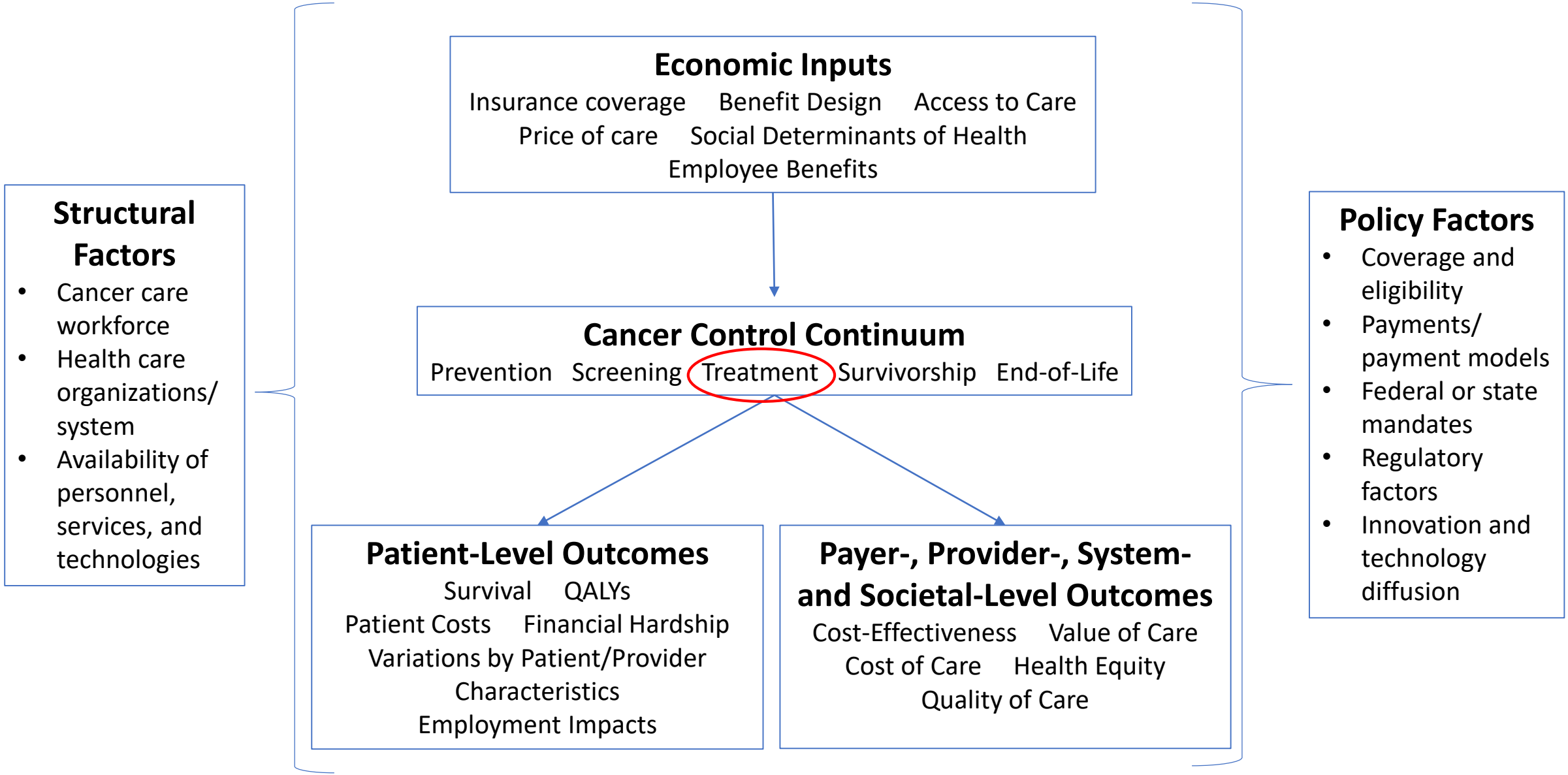
Conflicts of Interest

- DS:
  - Gave a talk at ESMO 2019 at Pfizer Satellite Symposium
  - Advised Grail on liquid biopsy tests 2020
  - Editorial fees from JAMA
  - Funding from AACR for Project Genie which gets funding from a variety of pharmaceutical firms
- JY
  - Boston scientific – speaking fees / consulting
  - Galera pharmaceuticals – advisory board

Outline of Talk

- Background
- Recommendations:
  - Data needs to expand cancer economics research capacity
  - Training needs to expand cancer economics impact
- Integrating economic endpoints into clinical trials

Health Economics Research Framework



Halpern et al. A framework for Cancer Health Economics Research. Cancer. 2021. https://acsjournals.onlinelibrary.wiley.com/doi/epdf/10.1002/cncr.33343

Background: Treatment

- Multiple types of cancer treatment (surgery, radiation therapy, systemic therapies) that vary by cancer site, stage, and molecular characteristics
- Cancer treatments are evolving rapidly
  - Novel treatments, including targeted therapies, rapidly introduced
  - Treatment intensity and duration increasing
- Cancer treatments are increasingly expensive
  - Insurers and payers need information about value
  - Patient financial hardship/toxicity a growing concern
  - Economic data especially relevant for decision making

Background: Treatment

- Many economic studies of cancer treatment use existing health insurance claims data and EHR data
- Data have limitations in terms of relevance and timeliness
  - Health insurance coverage benefit design rapidly changes
  - Data linkages (e.g., SEER-Medicare) provide information about cancer characteristics and treatment for select populations
  - Few prospective economic studies, including as part of clinical trials

Data limitations in conducting health economics research focused on cancer treatment: Unavailability of Key Measures

- Treatment eligibility measures
  - Functional and performance status
  - Molecular data
  - Treatment recommendations and factors affecting decision-making
- Key treatment outcomes
  - HRQOL, treatment-specific utility estimates, and other PROs
  - Treatment intent, reasons for switching, dose changes, and discontinuation
  - Recurrence, recurrence location, and recurrence timing
  - Survival and cause-specific mortality
- Other patient characteristics
  - Granularity on race/ethnicity
  - Sexual orientation and gender identity
  - Social determinants of health
- Non-medical economic data
  - Financial distress, food and housing insecurity
  - Productivity loss
- Provider characteristics

Absence of these measures limit observational studies as well as comparative studies of payment models

Data limitations in conducting health economics research focused on cancer treatment: Comprehensiveness

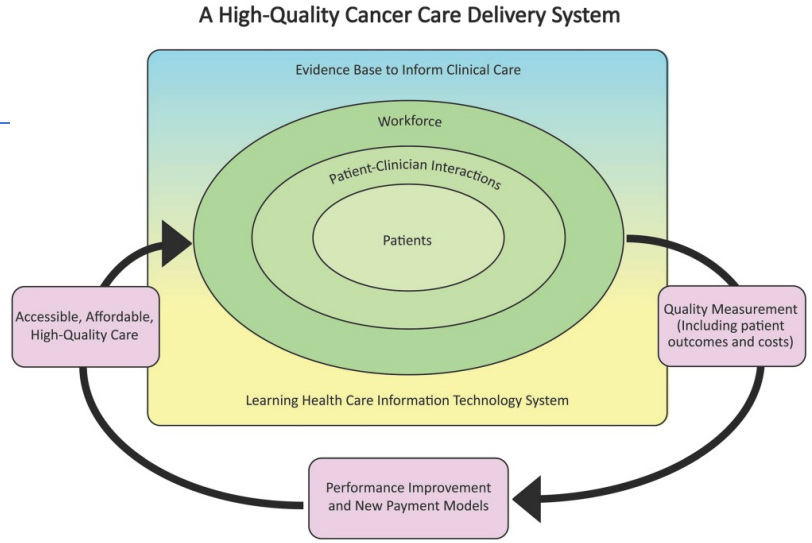
- Population-based data generally defined by geography, age, and insurance coverage type
- Detailed information about treatment and many outcomes end when health insurance coverage ends or changes, especially for <65 years without Medicare coverage
  - Median enrollment for Medicaid in 8 months
  - Transitions in coverage can be meaningful (switch to disability, unemployed due to cancer)
- Information about vital status frequently unavailable
- Area-level identifiers missing (e.g., zip code, census tract) and some vendors offer two versions of data requiring investigators to chose between key economic factors and other identifiers
- Caregiving data largely absent

Lack of comprehensive data limit understanding of disparities and evaluation of many outcomes in observational studies as well as comparative studies of payment models

Data limitations in conducting health economics research focused on cancer treatment: Timeliness

- Timeliness especially challenging with rapid changes in treatments
  - Tradeoffs between timeliness and representativeness
  - Data linkages provide rich data, but are even less timely
- Reliance on historical data less useful for research to inform changes in benefit design (e.g., high deductible health insurance plans, bundled payment, value-based payment)

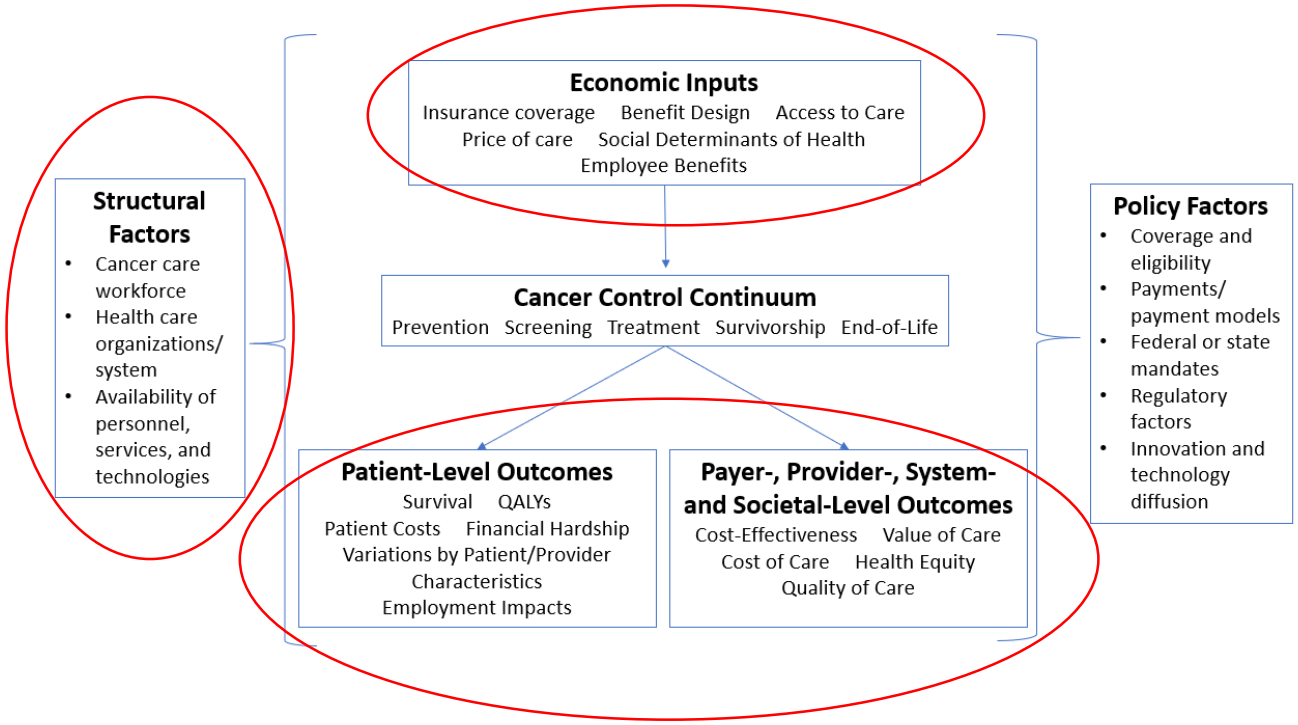
Lack of "real time" data means harder for research to inform policy and practice



Institute of Medicine Conceptual Model for a High-Quality Cancer Care Delivery System. Delivering High-Quality Cancer Care: Charting a New Course for a System in Crisis. Washington, DC: National Academies Press; 2013.

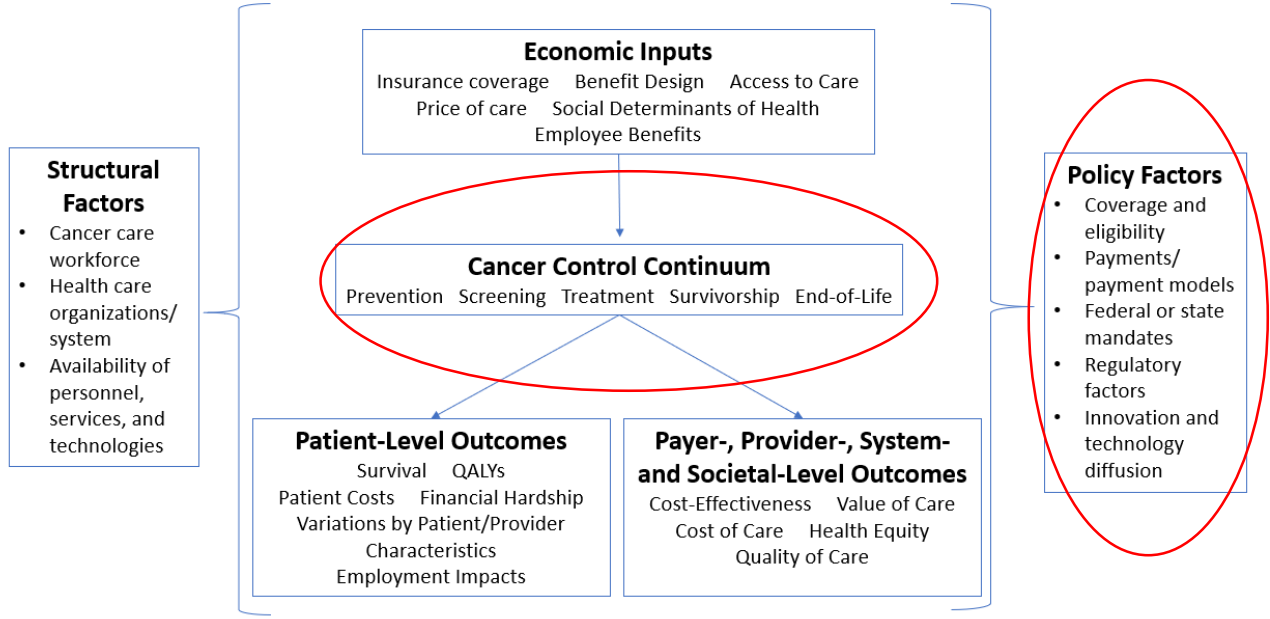
Training needs: For clinicians

- Health economics research requires multiple diverse skillsets
  - Economic analytic expertise is not taught in medical school – to understand and measure economic inputs and outcome
- Training intensity can vary depending on the end goal
  - Fellowship level training / K award for clinicians who are interested in a career in health economics
  - Health economics MPH programs
  - Policy issues can be learned in partnerships with clinical and advocacy groups
  - Meetings and seminars may help clinicians who want to collaborate without necessarily being the analytic engines for research



Training needs: For Health Services Researchers and Economists

- Clinical knowledge of cancer <u>treatment</u> is difficult to obtain
  - Knowledge of the rapidly changing cancer control continuum will likely require <u>partnering</u> with clinicians
  - Meetings and collaborative seminars may be optimal combination of efficiency and timeliness



Other opportunities for collaboration

- Meetings and Seminars to increase interactions
  - Sessions for cancer health economics research in clinical AND economic and health services research meetings
  - Annual or biennial meeting of cancer health economics
- Partnerships
  - CCDR within cooperative groups
  - Professional organizations (ASCO, Academy Health, ASHEcon)
  - Examples from Dissemination and Implementation Science
  - Collaboration in increasing utility of large datasets and research resources
    - Improve treatment and economic data available in large prospective cancer cohorts (e.g. add economic and behavior data to ASCO Cancer LinQ)
    - Including standardized economic data collection at baseline and follow-up

Economic Analyses Alongside Clinical Trials

Can this new treatment work?

RCTs still offer most unbiassed estimate of whether a treatment can work

What is the incremental value of this new treatment?

What does it cost to deliver this treatment?

Individual/Society	Direct Costs	Indirect Costs
Medical Costs	Immunotherapy MD visit	Premature death
Non-Medical Costs	Taxi to hospital Family caregiver	Sick leave Early retirement

Integrating Economic Analyses Alongside RCTS

Integrating Economic Analysis Into Cancer Clinical Trials: the National Cancer Institute–American Society of Clinical Oncology Economics Workbook

Introduction

Clinical economics is a new and evolving discipline that addresses the economic implications of changes in medical practice. As applied to cancer care, clinical economics assesses the costs and effectiveness of new cancer interventions and can be a valuable endpoint in selected clinical trials. Through the integration of economics into clinical evaluations, information can be developed that contributes to the decisions of patients, clinicians, health care managers, and policymakers as to the most effective allocation of cancer care resources.

To begin a formal effort to promote the development of economic analyses in National Cancer Institute (NCI) clinical trials, NCI sponsored a conference in 1994 with cancer center and cooperative group representatives to initiate discussions on the importance, appropriateness, and complexity of such evaluations. In 1995, the American Society of Clinical Oncology (ASCO) established its Health Economics Working Group with a charge to develop specific guidelines for implementing economic evaluations in cancer clinical trials. As a follow-up to these initiatives, in 1996, NCI and ASCO convened a workshop to consider the practical implementation of economic evaluations in cancer clinical trials. The participants in this small workshop included experts from cooperative groups, NCI staff, and other experts who are actively involved in health economics.

This workbook is the product of the meeting and subsequent discussions by the participants. It is meant to identify and elucidate the important characteristics of economic studies in the context of clinical trials, to indicate the considerations that investigators should address in their planning and implementation of such studies, and to suggest possible approaches. The workbook is neither a definitive text defining how all aspects of such studies should be handled nor an official NCI document prescribing how studies must be done. Rather, it is a developing guide to be used as a practical reference that will be revised as the state of the art progresses. The writing committee hopes that the workbook will serve as a useful tool for NCI cooperative groups as they incorporate economics as a research endpoint into the evaluation of new cancer treatment, prevention, and diagnosis strategies.

Part I: Economic Analysis and Cancer Clinical Trials

This section briefly presents the framework of economic theory underlying cost-effectiveness analysis and its application to the field of oncology. It is not, however, an in-depth review of the theory of economic evaluation, because many comprehensive sources currently exist *(1,2)*.

Why Economic Analysis?

The Rising Costs of Cancer Care

The percentage of total deaths in the United States attributable to cancer has risen from 16.3% in 1965 to 23.3% in 1997 *(3)*. From 1990 through 1996, the estimated costs of cancer treatment increased from $35 billion *(4)* to $50 billion due to higher inflation, increasing numbers of procedures and cases, and the aging of the population *(5)*. Even conservative estimates, measuring only the direct costs of treatment, show cost increases from $18.1 billion in 1985 to $27.5 billion in 1990 to $41.4 billion in 1994 *(6)*. Cancer will become the foremost cause of death in the United States by the end of the decade.

Statistics and predictions such as these underscore the likelihood that cancer will continue to absorb more of the increasingly limited resources of the U.S. health care system. Some researchers have suggested that increasing costs and demands from a sophisticated patient audience will require both implicit and explicit rationing *(7,8)*. In any event, economic forces will contribute to a growing need to better evaluate treatment practices by all clinicians, thus insuring that we utilize the relatively scarce resources of the health care system in an appropriate manner.

Cancer therapies are increasingly resource intensive, as evidenced by stem cell transplantation for hematologic disorders and solid tumors, paclitaxel for palliative chemotherapy of breast and ovarian cancers as well as non-small-cell lung cancer *(9)*, serotonin–antagonist antiemetics, and growth factors for supportive care during treatment. In an era of capitated physician and hospital payments, the resources available for cancer treatment will be increasingly constrained, and payers and purchasers will want to understand the value of cancer treatments, especially for resource-intensive therapies, before allowing widespread access to them. Furthermore, when health outcomes are identical for alternative therapies, the costs of these treatments may be the most important factor in determining whether to recommend or reimburse one of the treatments.

Encouraging examples of less intensive strategies have the potential to improve efficiency of cancer treatment, such as evidence-based, minimalist follow-up care for breast cancer patients *(10)*, decreased use of tumor markers in breast and colorectal cancers *(11)*, and conservative use of hematopoietic growth factors *(12)*, as well as a shift to less expensive outpatient treatments for stem cell transplantation *(13)*. However, these strategies remain a minority of cases of new treatments in oncology.

The Need to Improve Decision-Making

Because few medical interventions that provide health benefits also result in reduced health care expenditures (Table 1),

Is it worthwhile?

- Are anticipated differences in economic resource utilization meaningful from a societal perspective?
- Will adding an economic component influence clinical practice or health policy?
- Is collecting of good economic data feasible within the context of the overall trial design?
- Does the trial design have external validity from an economic perspective?

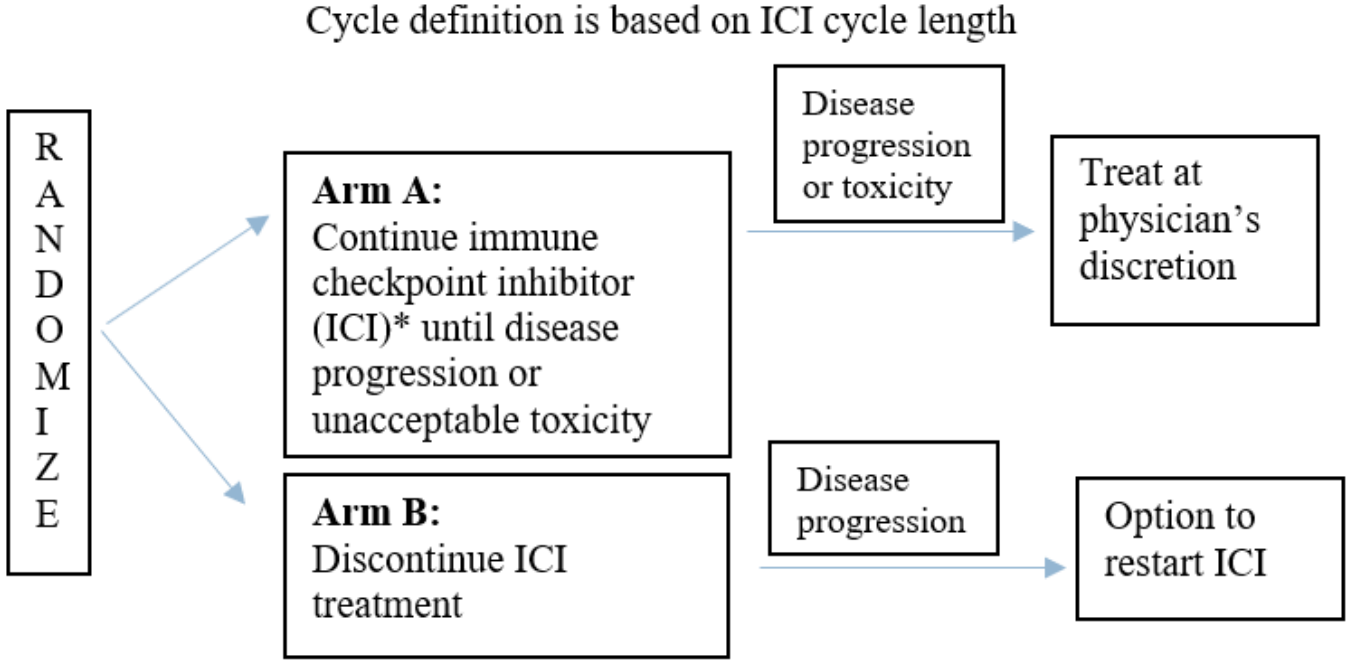
General Strategy:

- Capture baseline information on all participants
- Track resource utilization (big ticket items) for participants
- Estimate costs from resource utilization using CMS data
- Nice to add some indirect cost info with baseline data collection

Proposed Economic Companion May 2020:

What is the incremental cost-effectiveness of continuation of ICI therapy for patients with metastatic bladder cancer

Schema



Current state:

Infeasible to integrate economic companions alongside clinical trials

Reference Number: ***PA031901_O00PCONS01***
Protocol Consensus Review

Date: ***06/09/2020***
NCI Protocol #: ***A031901***
Local: ***A031901***
Version Date: ***05/04/2020***
Principal Investigator: ***Xiao X. Wei,* MD, Masters**

***Monica Marie Bertagnolli,* MD**
Alliance for Clinical Trials in Oncology
75 Francis Street
Boston, MA 02115

Dear ***Dr. Bertagnolli:***

Your Protocol, ***"Duration of Immune Checkpoint Therapy in Locally Advanced or Metastatic Urothelial Carcinoma: A Randomized Phase 3 Non-Inferiority Trial,"*** NCI Document # **A031901**, was reviewed by The Protocol Review Committee (PRC) of the Cancer Therapy Evaluation Program (CTEP) on ***05/28/2020***. The PRC requests that you address the comments in the enclosed Consensus Review. Each comment falls into one of the following categories:

- **Comments from CTEP or Pharmaceutical Collaborator requiring a Response:** For each comment, please make suitable revisions in the protocol; or, if you disagree with the reviewers, provide the reasons for not making the suggested revision(s) in the summary of changes that accompanies the revised protocol.
- **Recommendations from CTEP or Pharmaceutical Collaborator:** These comments are advisory and you are not obligated to make these changes. However, the PRC requests that you consider whether they would improve your study.

In the summary of changes embedded in your revised protocol, please address each numbered comment point by point. Your response to each comment should appear in **bold** directly below the specific comment from the Consensus Review. Include the section(s) where the changes are located in the revised protocol or informed consent and hyperlink them to comply with CTEP's electronic submission policy. A copy of the informed consent (regardless of whether changes have been made to it or not) must be submitted. **All changes to the protocol or informed consent must be detailed in the summary of changes. Submissions that do not respond point by point will be returned to the Investigator without re-review. Please be advised that changes to the protocol outside of those requested by NCI may delay re-review and could jeopardize activation by the OEWG deadline.**

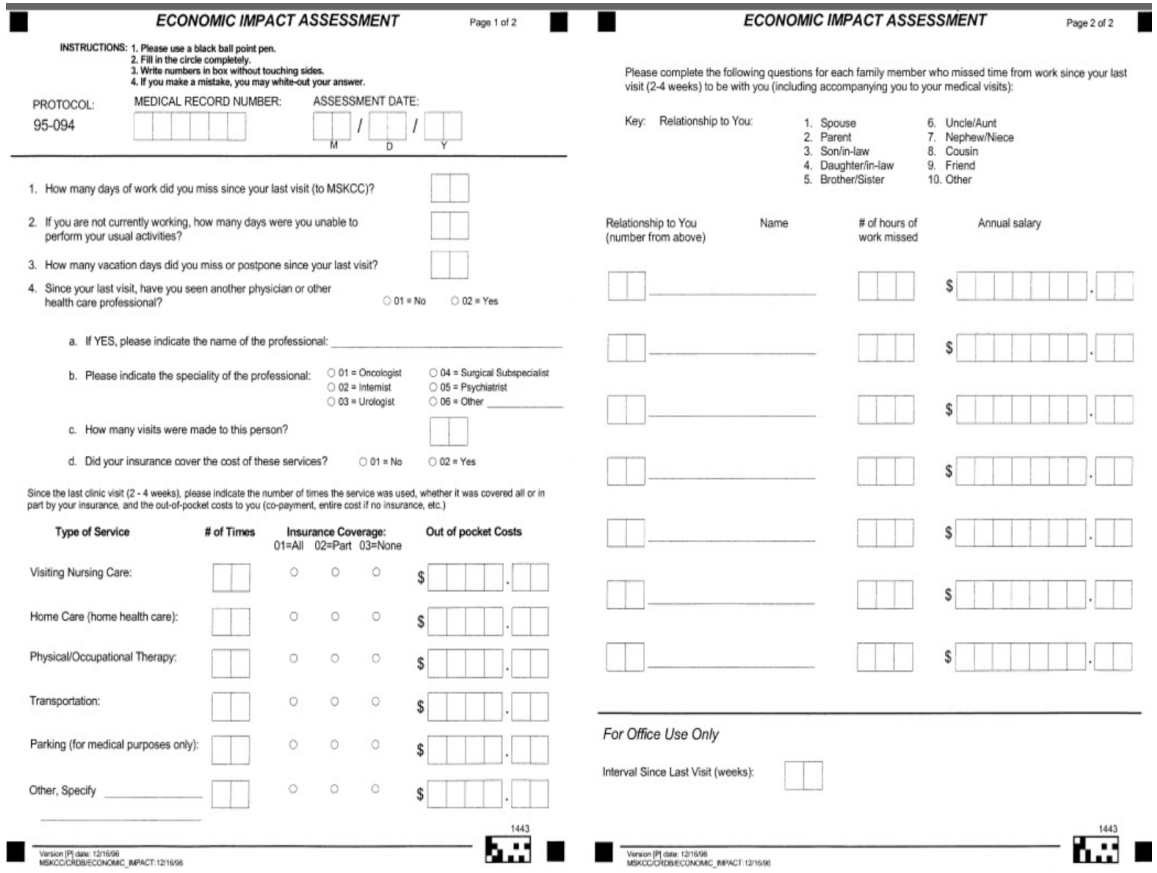
In addition, an unofficial copy of the protocol with administrative comments already inserted into the protocol or informed consent via Track Changes may be attached. The comments inserted into the unofficial copy of the protocol or informed consent have been highlighted in yellow in the section field of the consensus review for easy identification between the two documents. To respond to those changes that

		PI response:
5.	14.1.1, 14.1.2, 14.1.3	The investigators noted the inclusion of health economics and healthcare utilization. Both should be deleted from the protocol. Neither CTEP nor DCP provides funding for these studies. **PI response:**

Are Cost Effective Analysis (CEA) studies eligible for BIQSFP funding?

NO… CEA studies are no longer eligible for BIQSFP funding. NCI is exploring other mechanisms through which CEA studies may be supported, outside the BIQSFP program.

Strategies to Get Economic Data on Indirect Costs Exist



ECONOMIC IMPACT ASSESSMENT Page 1 of 2

INSTRUCTIONS: 1. Please use a black ball point pen.
2. Fill in the circle completely.
3. Write numbers in box without touching sides.
4. If you make a mistake, you may white-out your answer.

PROTOCOL: 95-094 MEDICAL RECORD NUMBER: ASSESSMENT DATE: M / D / Y

1. How many days of work did you miss since your last visit (to MSKCC)?
2. If you are not currently working, how many days were you unable to perform your usual activities?
3. How many vacation days did you miss or postpone since your last visit?
4. Since your last visit, have you seen another physician or other health care professional? ○ 01 = No ○ 02 = Yes

a. If YES, please indicate the name of the professional: _____

b. Please indicate the speciality of the professional: ○ 01 = Oncologist ○ 02 = Internist ○ 03 = Urologist ○ 04 = Surgical Subspecialist ○ 05 = Psychiatrist ○ 06 = Other _____

c. How many visits were made to this person?

d. Did your insurance cover the cost of these services? ○ 01 = No ○ 02 = Yes

Since the last clinic visit (2 - 4 weeks), please indicate the number of times the service was used, whether it was covered all or in part by your insurance, and the out-of-pocket costs to you (co-payment, entire cost if no insurance, etc.)

Type of Service	# of Times	Insurance Coverage: 01=All 02=Part 03=None	Out of pocket Costs
Visiting Nursing Care:		○ ○ ○	$
Home Care (home health care):		○ ○ ○	$
Physical/Occupational Therapy:		○ ○ ○	$
Transportation:		○ ○ ○	$
Parking (for medical purposes only):		○ ○ ○	$
Other, Specify _____		○ ○ ○	$

1443

Version [P] date: 12/16/96
MSKCC/CRDB/ECONOMIC_IMPACT.12/16/96

ECONOMIC IMPACT ASSESSMENT Page 2 of 2

Please complete the following questions for each family member who missed time from work since your last visit (2-4 weeks) to be with you (including accompanying you to your medical visits):

Key: Relationship to You:
1. Spouse
2. Parent
3. Son/in-law
4. Daughter/in-law
5. Brother/Sister
6. Uncle/Aunt
7. Nephew/Niece
8. Cousin
9. Friend
10. Other

Relationship to You (number from above)	Name	# of hours of work missed	Annual salary
	_____		$
	_____		$
	_____		$
	_____		$
	_____		$
	_____		$
	_____		$

For Office Use Only

Interval Since Last Visit (weeks):

1443

Version [P] date: 12/16/96
MSKCC/CRDB/ECONOMIC_IMPACT.12/16/96

Direct Medical Costs	Resource Utilization from EHRs or Patient Reporting Use Administrative data to estimate costs
Indirect medical costs	Surveys of trial participants (with consistent elements across studies)
Indirect costs	New data linkages Surveys of trial participants/caregivers

What would transform the ability to evaluate the economics of cancer treatment?

The Fundamental Research Question	Transformational Intervention	Desired State/Outcome
What is the ICER of Treatment A vs. Treatment B?	Provide clear mechanism to support integration of economic analyses alongside clinical trials	Straightforward to integrate CEA into relevant RCTs Cross-trial comparisons are possible
What does it cost the health system to deliver 1 month, 1 year, typical course of this treatment?	Develop standard methods that facilitate comparisons across treatments	Costs for delivering standardized units of all cancer treatments are available in league tables---downstream pressure on prices
What does it cost the patient to obtain 1 mo, 1 year, typical course of this treatment in terms of *time*?	Develop/deploy standard methods to estimate the economic burden of treatment. Eg: 4 visits, 16 hours per month	Patients have access to clear information about what it takes to get a specific treatment over standardized courses
What does it cost the patient to obtain 1 mo, yr, typical course of this treatment in terms of $$	Develop/deploy standards based on CMS pricing and average co-pay/coinsurance.	Patients have access to clear information about what it costs to get a treatment over standardized courses (adjustable based on plan-specific cost-sharing requirements)
What does it cost society to have patients get this treatment with respect to productivity?	Develop/deploy standard methods to estimate missed work/return to work usual activities	Society and employers paying for Rx are able to compare treatments in terms of anticipated lost productivity
How do economic factors influence treatment outcomes?	Deploy standardized evaluations that include Social Determinants of Health for all trial participants—more important than the bilirubin and CTCAE grading!	The risk of disparate outcomes can be identified from RCT experience and remediation strategies introduced to mitigate risk of exacerbating disparities

Thanks!

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