CCTG NEW INVESTIGATOR CTC 2019: ECONOMICS WORKSHOP

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OUTLINE

- METHODS OF EVALUATION
- COSTS
- EFFECTS
- UNCERTAINTY
- SAMPLE SIZE
- EXAMPLES

Methods for Economic Evaluation

Evaluation method	Outcome Valuation
Cost-minimization $\Delta_e \sim 0$	Multiple outcomes in natural units – examine cost difference between equivalent therapies.
Cost-effectiveness $\Delta_e > 0$	Evaluate of efficiency/effectiveness of a new therapy– Additional cost per unit of gained benefit (LYs)
Cost-utility $\Delta_e > 0$	Multiple outcomes combined: Additional cost per unit of gained of the adjusted benefit (e.g., QALYs)
Cost-benefit $\Delta_e > 0$	Net monetary benefit (NMB)

Cost Effectiveness Analysis

- Cost Effectiveness Analysis (CEA) is a type of economic evaluation that examine both the costs and outcomes of alternative therapies.
- Costs are expressed in monetary terms
- Benefits are expressed in “natural units” of health outcome, e.g., “cases prevented”, “life-years saved”, etc.
- Measure of cost-effectiveness of new over standard: Incremental Cost Effectiveness Ratio (ICER) -> $\Delta C/\Delta E$; e.g. incremental Cost divided by additional life-years gained (or other measure of benefit)

Cost Utility Analysis

- Costs are expressed in monetary terms
- Benefits are expressed in quality-adjusted "natural units," e.g., quality adjusted life-years
- Incremental Cost Utility Ratio (ICUR) -> Incremental Cost divided by Incremental Quality Adjusted Life Years gained

Steps in Economic evaluation

- Quantify the Cost of care
- Quantify outcomes
- Assess whether and by how much average costs and outcomes differ among the treatment groups
- Estimate and Compare magnitude of difference in costs and outcomes and evaluate “value for cost” (e.g. a cost-effectiveness ratio)
- Evaluate sampling uncertainty and perform sensitivity analysis
- Assessing ICER as a function of the Social Value of health – the Cost Effective Acceptability Curve

Quantify the Cost of care

- Cost ((in term of amount of money)

  -- Direct medical costs (Drugs, Hospitalization, Physicians and other medical care givers, Lab testing, et al.)

  -- Direct Non-medical costs (Travel and accommodation, family care, et al.)

  -- Indirect Costs: Cost of lost or reduced productivity resulting from morbidity or premature mortality due to a medical condition or treatment (Work loss, lost productivity at work, premature death)

  -- Intangible costs: Cost assigned to amount of suffering due to the disease or treatment (Pain, inconvenience, suffering et al.)

2. OUTPATIENT LOG

In the past 4 weeks, has the patient had any outpatient visits, treatments or procedures? (Only provide information for visits not required by the study protocol.)

___ No ___ Yes → if yes, please complete the table below.

Provider Type	Office/Clinic Visits (#)	Home Visits (#)	
Oncologist			
Radiation Oncologist			
Surgeon			Emergency Room Visits (#)
Other Specialist			
Primary Care Physician			_____
Psychiatrist			
Psychologist			
Physical Therapist			
Other: _____			

Outpatient Procedures/Treatments

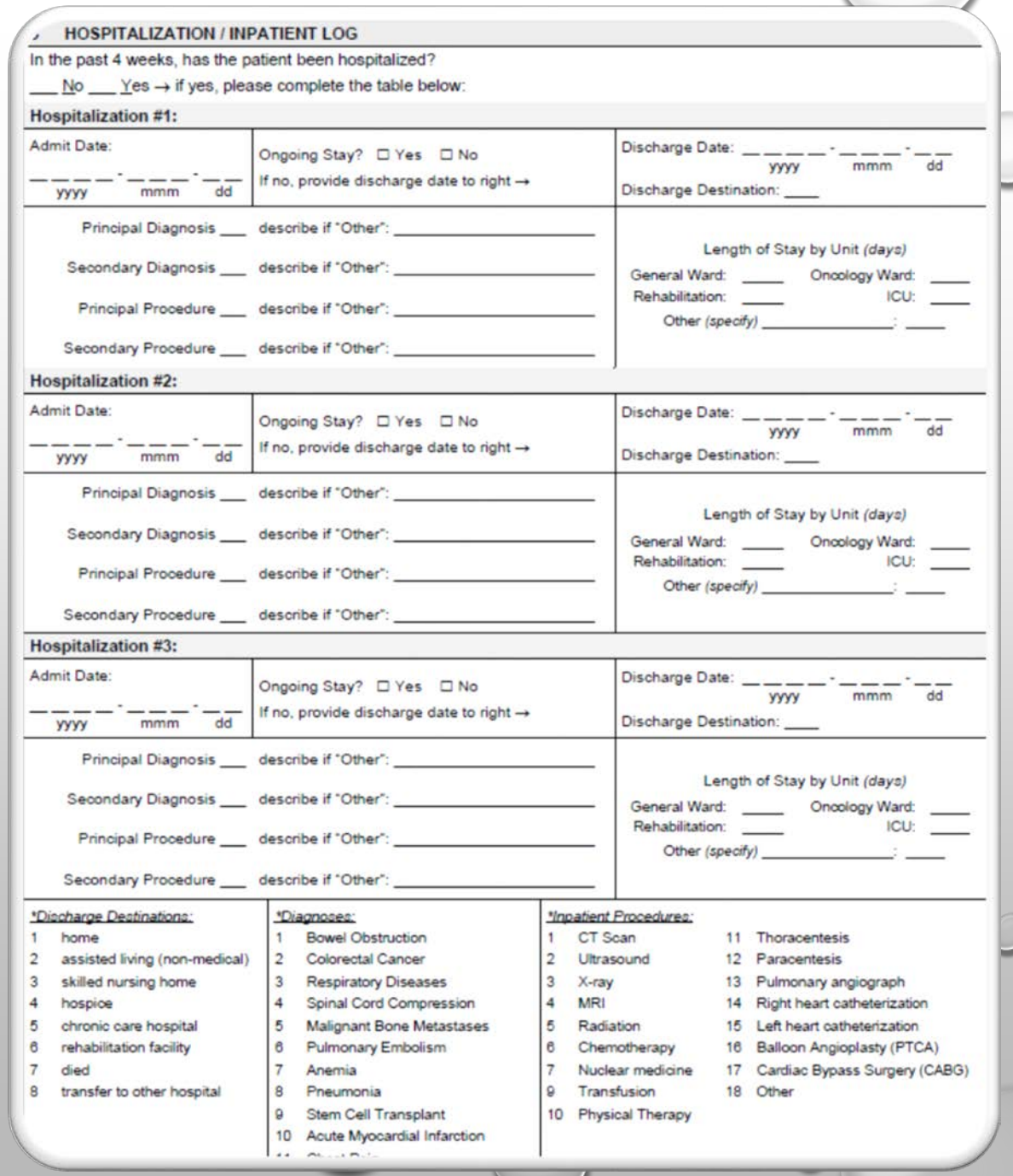
Type* (enter #)	Quantity	Describe if "Other" or "Chemotherapy"
	_____	
	_____	
	_____	
	_____	
	_____	
	_____	

**Outpatient Procedure/Treatments:*

1 CT Scan
2 Ultrasound
3 X-ray
4 MRI
5 Nuclear medicine
6 Transfusion *(for quantity, provide number of units)*
7 Thoracentesis
8 Paracentesis
9 Other
10 Patient-controlled analgesia pump *(for quantity, provide number of days)*
11 Radiation; *(for quantity, provide number of weekly treatments)*
12 Chemotherapy *(for quantity, provide number of cycles)*

CO.17 RUA

CO.17 RUA



HOSPITALIZATION / INPATIENT LOG

In the past 4 weeks, has the patient been hospitalized?

___ No ___ Yes → if yes, please complete the table below:

Hospitalization #1:

Admit Date: __ __ __ __ - __ __ - __ __ (yyyy mmm dd)	Ongoing Stay? ☐ Yes ☐ No If no, provide discharge date to right →	Discharge Date: __ __ __ __ - __ __ - __ __ (yyyy mmm dd) Discharge Destination: ____
Principal Diagnosis ___ describe if "Other": _____ Secondary Diagnosis ___ describe if "Other": _____ Principal Procedure ___ describe if "Other": _____ Secondary Procedure ___ describe if "Other": _____		Length of Stay by Unit *(days)* General Ward: ____ Oncology Ward: ____ Rehabilitation: ____ ICU: ____ Other *(specify)* _____: ____

Hospitalization #2:

Admit Date: __ __ __ __ - __ __ - __ __ (yyyy mmm dd)	Ongoing Stay? ☐ Yes ☐ No If no, provide discharge date to right →	Discharge Date: __ __ __ __ - __ __ - __ __ (yyyy mmm dd) Discharge Destination: ____
Principal Diagnosis ___ describe if "Other": _____ Secondary Diagnosis ___ describe if "Other": _____ Principal Procedure ___ describe if "Other": _____ Secondary Procedure ___ describe if "Other": _____		Length of Stay by Unit *(days)* General Ward: ____ Oncology Ward: ____ Rehabilitation: ____ ICU: ____ Other *(specify)* _____: ____

Hospitalization #3:

Admit Date: __ __ __ __ - __ __ - __ __ (yyyy mmm dd)	Ongoing Stay? ☐ Yes ☐ No If no, provide discharge date to right →	Discharge Date: __ __ __ __ - __ __ - __ __ (yyyy mmm dd) Discharge Destination: ____
Principal Diagnosis ___ describe if "Other": _____ Secondary Diagnosis ___ describe if "Other": _____ Principal Procedure ___ describe if "Other": _____ Secondary Procedure ___ describe if "Other": _____		Length of Stay by Unit *(days)* General Ward: ____ Oncology Ward: ____ Rehabilitation: ____ ICU: ____ Other *(specify)* _____: ____

Discharge Destinations:

1 home
2 assisted living (non-medical)
3 skilled nursing home
4 hospice
5 chronic care hospital
6 rehabilitation facility
7 died
8 transfer to other hospital

Diagnoses:

1 Bowel Obstruction
2 Colorectal Cancer
3 Respiratory Diseases
4 Spinal Cord Compression
5 Malignant Bone Metastases
6 Pulmonary Embolism
7 Anemia
8 Pneumonia
9 Stem Cell Transplant
10 Acute Myocardial Infarction

Inpatient Procedures:

1 CT Scan
2 Ultrasound
3 X-ray
4 MRI
5 Radiation
6 Chemotherapy
7 Nuclear medicine
9 Transfusion
10 Physical Therapy
11 Thoracentesis
12 Paracentesis
13 Pulmonary angiograph
14 Right heart catheterization
15 Left heart catheterization
16 Balloon Angioplasty (PTCA)
17 Cardiac Bypass Surgery (CABG)
18 Other

BASELINE

Lost Productivity Questionnaire – ENGLISH

NCIC CTG Trial: LY.12

This page only to be completed by the Clinical Research Associate

Patient Information

NCIC CTG Patient Serial No: _____ Hospital No.: _____ *(optional, if approved by REB)* Patient Initials: ___ ___ ___ (first-middle-last)

Institution: _____ Investigator: _____

Please obtain this lost productivity assessment at baseline
(day 1 of cycle 1, or within 2 weeks prior to that date).

Date questionnaire completed: __ __ __ __ - __ __ __ - __ __
yyyy mmm dd

General Questions

1) What type of medical insurance do you currently have?

(Check ✓ all that apply.)

- ☐ Provincial health insurance
- ☐ Individual/ group health
- ☐ Other (specify): _____

2) If you are working for pay or have done paid work in the past, what would best describe your field of employment? *(Check ✓ one only. Choose your most recent employment; if more than one paid job at once, choose the employment involving the most time commitment.)*

- ☐ Management
- ☐ Business/ finance/ administrative
- ☐ Natural and applied sciences
- ☐ Health services
- ☐ Education
- ☐ Government services
- ☐ Social science
- ☐ Religion
- ☐ Art/culture
- ☐ Recreation and/or sport
- ☐ Sales and/or service
- ☐ Trades/ transport/ construction
- ☐ Primary industry
- ☐ Processing/manufacturing/utilities
- ☐ Other (specify): _____
- ☐ Not applicable; no paid work

COMMENTS : _____

_____

3) Which of the following best describes your work status at this time?

(Check ✓ one only.)

- ☐ Working full-time for pay (> 30 hours per week) -- (includes self-employed)
- ☐ Working part-time for pay (≤ 30 hours per week) -- (includes self-employed)
- ☐ On sick leave from full- or part-time work: (Date leave started: _____) (Year – Month – Day)
- ☐ On disability leave from full- or part-time work: (Date leave started: _____) (Year – Month – Day)
- ☐ Unemployed
- ☐ Retired
- ☐ Homemaker/ Stay at home parent or caregiver
- ☐ Other, specify _____

4) *In the last 3 weeks*, has there been any change in your work status compared to before that?

(Check ✓ one only.)

- ☐ No, no change
- ☐ Yes, started working full time hours (> 30 hours per week)
- ☐ Yes, started working part time hours (≤ 30 hours per week)
- ☐ Yes, started sick or disability leave: (Date leave started: _____) (Year – Month – Day)
- ☐ Yes, quit work/ became unemployed or retired: (Date started: _____) (Year – Month – Day)
- ☐ Yes ,other: specify _____

5) *In the last 3 weeks*, how much time have you been unproductive (unable to work or do usual household activities) due to not feeling well, receiving treatment and/ or being in hospital for your lymphoma?

(Check ✓ one only.) Estimate to the nearest ½ day; assume 1 day is 8 hours.

- ☐ none (0 days)
- ☐ < 1 day (specify # of hours: _____)
- ☐ 1 to 3 days (specify # of days: _____)
- ☐ More than 3 days (specify # of days _____)
- ☐ Don't know – can't remember

6) *In the last 3 weeks*, how much paid work time have you missed due to illness, treatment and/ or being in hospital for your lymphoma?

(Check ✓one only.) Estimate to the nearest ½ day; assume 1 day is 8 hours.

- ☐ none (0 days)
- ☐ < 1 day (specify # of hours: _____)
- ☐ 1 to 3 days (specify # of days: _____)
- ☐ More than 3 days (specify # of days _____)
- ☐ Not applicable – not currently working
- ☐ Don't know – can't remember

7) Please rate your activity level on average *in the last 3 weeks* (circle applicable number):

0	1	2	3	4	5	6	7	8	9	10
Exhausted in bed all day										Normal activity level

Paid Assistance and Professional Care for Your Lymphoma

8) *In the last 3 weeks*, how much paid health and/ or home worker time have you needed? (Examples include a home visiting nurse or someone to do blood work, VON, home care worker.)

(Check ✓one only.) Estimate to the nearest ½ day; assume 1 day is 8 hours.

- ☐ none (0 days)
- ☐ < 1 day (specify # of hours: _____ and also the # of visits involved: _____)
- ☐ 1 to 3 days (specify # of days: _____ and also the # of visits involved: _____)
- ☐ More than 3 days (specify # of days: _____ and also the # of visits involved: _____)
- ☐ Don't know – can't remember

9) *In the last 3 weeks*, how much other paid assistance have you needed? (Examples include a translator to attend doctor visits, a driver to take you to appointments).

(Check ✓one only.) Estimate to the nearest ½ day; assume 1 day is 8 hours.

- ☐ none (0 days)
- ☐ < 1 day (specify # of hours: _____) Specify type of assistance: _____
- ☐ 1 to 3 days (specify # of days: _____) Specify type of assistance: _____
- ☐ More than 3 days (specify # of days: _____) Specify type of assistance: _____
- ☐ Don't know – can't remember

Unpaid Caregiver(s)

10) *In the last 3 weeks*, who has primarily helped to look after your needs without formal pay?

(Check ✓all that apply.)

- ☐ No one (no unpaid caregiver)
- ☐ Spouse
- ☐ Child/Parent
- ☐ Other relative
- ☐ Friend
- ☐ Neighbor
- ☐ Other (specify) _____

11) *In the last 3 weeks*, how much time has your unpaid caregiver(s) helped you?

(Check ✓one only.) Estimate to the nearest ½ day; assume 1 day is 8 hours.

- ☐ none (0 days)
- ☐ < 1 day (specify # of hours: _____)
- ☐ 1 to 3 days (specify # of days: _____)
- ☐ More than 3 days (specify # of days: _____)
- ☐ Don't know – can't remember
- ☐ Not applicable – I have no unpaid caregiver(s)

12) *In the last 3 weeks*, how many paid work days at his or her paying job(s) has your unpaid caregiver(s) missed in order to help you?

(Check ✓one only.) Estimate to the nearest ½ day; assume 1 day is 8 hours.

- ☐ none (0 days)
- ☐ < 1 day (specify # of hours: _____)
- ☐ 1 to 3 days (specify # of days: _____)
- ☐ More than 3 days (specify # of day: _____)
- ☐ Don't know
- ☐ Not applicable – no unpaid caregiver(s) or unpaid caregiver(s) not currently working for pay

Quantify the Cost of care

- Discounting of Costs

-- A procedure used in economic analysis to express as “present values” those costs and benefits that will occur in future years

1. Individuals prefer to receive benefit today rather than future

2. Resource invested today in alternative programs could earn a return over time

3. Range from 0 to 10%, 3% and 5% are commonly used

Quantify outcomes (Effects)

- Primary endpoint of clinical trials: Practice changing outcomes.
- Different disease setting with different outcomes

  -- e.g. Cancer clinical trial, overall survival, Disease relapse free survival, et al.
- Summary statistic of efficacy (relative difference) used in Clinical trial may be different that of effect (Absolute difference) in economic evaluation.
- Summary statistic for economic evaluation: Mean in unit of effectiveness.(Restricted mean, AUC of K-M curves for OS)

Summary statistic of effectiveness

- Summary statistic for economic evaluation:

  Mean of effectiveness.
- Composite endpoints: e.g. time to event /Binary endpoint with fatal and nonfatal events

  -- Different outcomes are rarely of equal importance: Weighting endpoints, weighted average
- QALYs: Weighting the time in different health states: e.g. Cancer clinical trial, time with toxicities, time without toxicities and disease progress, time with progressed disease. Summary statistic for economic evaluation: Weighted (Utility index, EQ5) average of time in each health state.

Health Utilities Index Mark 3 (HUI3) Questionnaire (CO.17)

17 QUESTIONS/8 DIMENSIONS (~10 MINS)

- READING
- RECOGNIZING OTHERS
- HEARING (GROUP VS 1:1)
- BEING UNDERSTOOD (STRANGERS VS FRIEND)
- PAIN
- WALKING
- USE OF HANDS
- MEMORY
- THINKING/PROBLEM SOLVING
- ADL
- GENERAL WELLNESS

EQ-5D Questionnaire – ENGLISH

NCIC CTG Trial: **BL.12**

This **page** to be completed by the Clinical Research Associate

Patient Information

NCIC CTG Patient Serial No: _____ Patient Initials: ____ ____ ____
(first-middle-last)

Institution: _____ Investigator: _____

Scheduled time to obtain EQ-5D Questionnaire- please check (✓)

☐ Prior to randomization

During chemotherapy:

☐ Days 5 - 7 cycle 1 ☐ Days 5 - 7 cycle 2 ☐ Day 1 cycle 4 ☐ Day 1 cycle 8 ☐ Day 1 cycle 12

☐ Day 1 cycle 16 ☐ Day 1 cycle 20 ☐ Day 1 cycle 24 ☐ Day 1 cycle 28 ☐ Day 1 cycle _____

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY
- I have no problems in walking about ❑
- I have slight problems in walking about ❑
- I have moderate problems in walking about ❑
- I have severe problems in walking about ❑
- I am unable to walk about ❑

SELF-CARE
- I have no problems washing or dressing myself ❑
- I have slight problems washing or dressing myself ❑
- I have moderate problems washing or dressing myself ❑
- I have severe problems washing or dressing myself ❑
- I am unable to wash or dress myself ❑

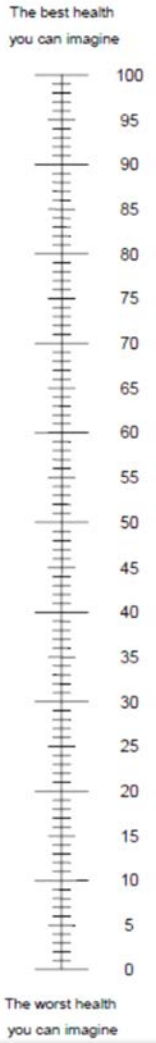
USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*
- I have no problems doing my usual activities ❑
- I have slight problems doing my usual activities ❑
- I have moderate problems doing my usual activities ❑
- I have severe problems doing my usual activities ❑
- I am unable to do my usual activities ❑

PAIN / DISCOMFORT
- I have no pain or discomfort ❑
- I have slight pain or discomfort ❑
- I have moderate pain or discomfort ❑
- I have severe pain or discomfort ❑
- I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION
- I am not anxious or depressed ❑
- I am slightly anxious or depressed ❑
- I am moderately anxious or depressed ❑
- I am severely anxious or depressed ❑
- I am extremely anxious or depressed ❑

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine. 0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐

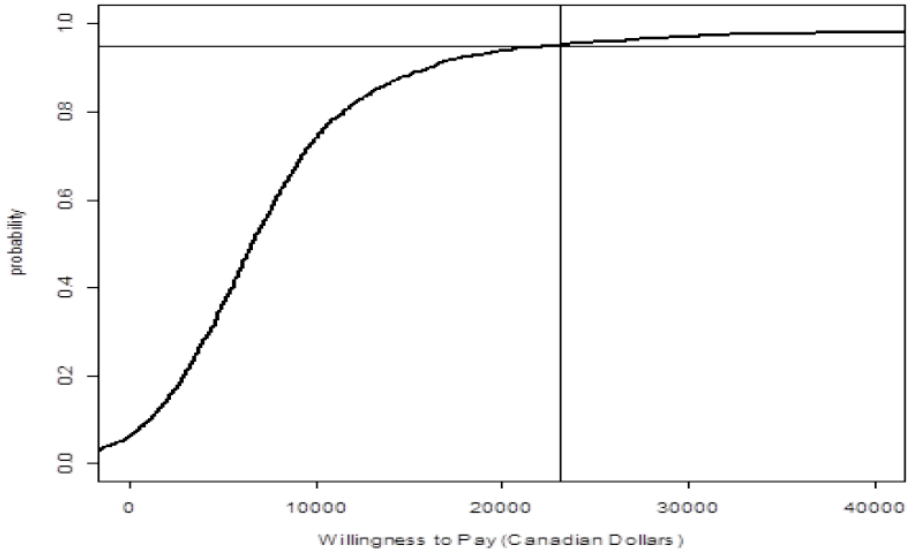


5 DIMENSIONS (~ 2 MINS)

Assessment of uncertainty: Cost Effectiveness Acceptability Curves

- Conduct bootstrap simulation
- Examine all results that fall within 95% confidence intervals for the cost effectiveness ratio
- Compare to reference values for social value of health (V_s) (The value that a society willing to pay for one extra unit of health. It reflects the a society's level of economic wealth and the relative distribution of that wealth to the health sector)
- Calculate probability that: ICER < V_s

Cost Effectiveness Acceptability Curves



Assessment of uncertainty: Sensitivity analysis

- To ascertain how the model depends upon the information fed to it.
- Changing efficacy values (Use Discounted LYs, QALY instead of LYs, or reduce the LYs by certain percentage) and costs (Increase or decrease certain proponent of costs at certain percentage) to see whether change had a significant effect on ICER (point estimate, and 95% C.I.). Identify driving force for ICER.

Not secure | statapps.tk/icer_samplesize/

Apps | Mail - nreaume@to... | SharePoint | Files - OneDrive | Evernote | TweetDeck | Citrix Receiver | CBC.ca | World at Six | Ottawa, Ontario - 7... | E-Journals A-Z | Other bookmar

Samplesize for Health Economic in Clinical Trials

Willingness-to-pay (in $K or $M)

0.5 — 15 — 50

Cost for control and treatment arms (in $K or $M)

0 — 20 — 28 — 100

SD for control and treatment costs (in $K or $M)

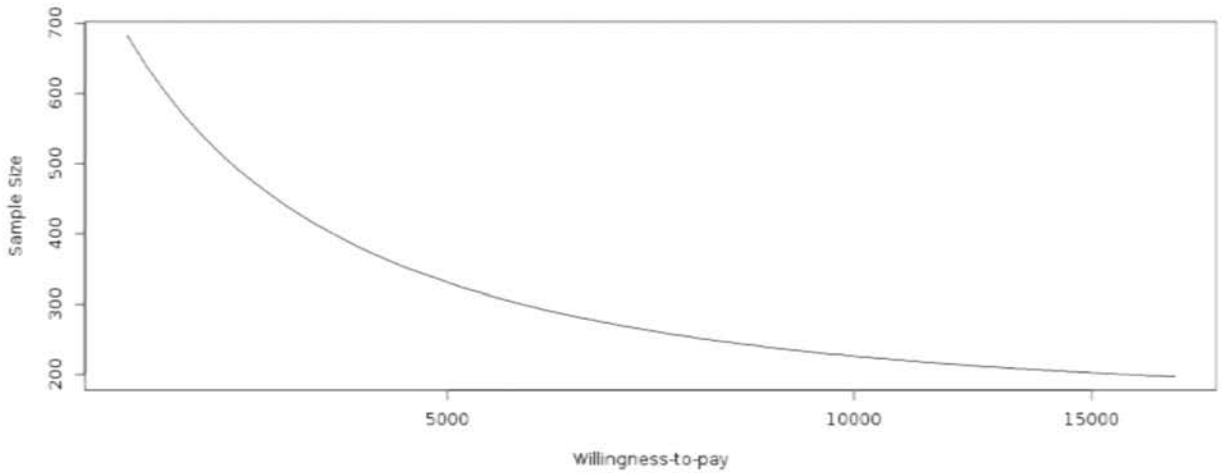
0 — 8 — 100

Hazards ratio

0.05 — 0.67 — 0.95

Optional controls

Default



Summary

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Willingness-to-pay for one year of life gain is  15000 dollors for this study.
One-sided Alpaha =  0.05 Power =  80 %. Correlation coefficient between net benefit and net cost = 0
Survival distribution: 4 year survival rate =  70 %.
Sample size =  202
ICER = 1448.316 dollors per year of life gain.
One-sided ICER upper 95  % CI:  3670.702 dollors.
Upper bound of CI / ICER = 2.53
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A RANDOMIZED PHASE III STUDY OF DURATION OF ANTI-PD-1 THERAPY IN METASTATIC MELANOMA (STOP-GAP)
CCTG PROTOCOL NUMBER: **ME.13**

2.5 Economic Evaluation

Patient outcomes will be prospectively compared in all randomized patients. The aim of the economic evaluation is to assess heath care utilization in the context of quality-adjusted survival outcomes, and thus understand the potential tradeoffs of these competing treatment approaches. Cost-effectiveness and cost-utility analyses will be conducted to compare the overall cost per life-year and per quality-adjusted-life-year (QALY) for the 2 groups. The collection of economic data in this setting is of interest given a government funded health care system with limited resources for covering the cost of expensive cancer therapy. The perspective of this evaluation will be that of the government as payer in a universal access health care system.

Case report forms will be used to document non-protocol driven health care resource utilization related to therapy over the course of treatment and follow-up, including outpatient consultations/visits for PD-1 inhibitor administration, supportive care medications for management of toxicity, investigations/admissions/treatment of adverse events and disease progression, and all emergency room and home care visits. Unit costs will be ascertained from provincial sources in adjusted Canadian dollars. Forms will be collected at 3-month intervals from randomization until disease progression or termination of study.

Patient preferences, or utilities, will be derived from the EQ-5D questionnaire *[Brooks 1996; Drummond 1997; www.euroqol.org]*.The EQ-5D self-administered questionnaire consists of two pages comprising the EQ-5D descriptive system and the EQ VAS. The EQ-5D descriptive system comprises five dimensions of health (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and each dimension comprises three levels (no problems, some/moderate problems, extreme problems). The five level score may also be used. A unique EQ-5D health state is defined by combining one level from each of the five dimensions. The EQ VAS records the respondent's self-rated health status on a vertical graduated (0-100) visual analogue scale. The EQ-5D is a validated instrument that has been used in population surveys and clinical trial settings. Analysis will be performed as detailed in the statistical section of the protocol (Section 13). EQ-5D will be obtained at intervals outlined in Section 5.

CANADIAN CANCER TRIALS GROUP (CCTG)

A PHASE III TRIAL OF STEREOTACTIC RADIOSURGERY COMPARED WITH WHOLE BRAIN RADIOTHERAPY (WBRT) FOR 5-15 BRAIN METASTASES

CCTG Protocol Number: **CE.7**
ALLIANCE Protocol Number: **CE.7**

Study Exempt from IND Requirements per 21 CFR 312.2(b)

CCTG STUDY CHAIR:	David Roberge
ALLIANCE STUDY CHAIR:	Michael Chan
TRIAL COMMITTEE:	Paul Brown Warren Mason Anthony Whitton
SENIOR INVESTIGATOR:	Chris O'Callaghan
BIOSTATISTICIAN:	Keyue Ding
QUALITY OF LIFE COORDINATOR:	Anne Leis
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QUESTIONS?

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