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Health Economics

New Investigators Course

22 August 2024

Dr. Annette Hay

Professor, Queen's University

Thanks to Natasha Leighl, Nicole Mittmann, Neal Reaume & Matt Cheung for contributed slides

Conflicts of Interest – research funding

- Roche
- AbbVie
- Celgene
- Merck
- Seattle Genetics
- Novartis
- Karyopharm
- Janssen

Objectives

- To consider what trial settings are appropriate for health economic analyses
- To discuss the components of health economic analyses

Value in Health Care

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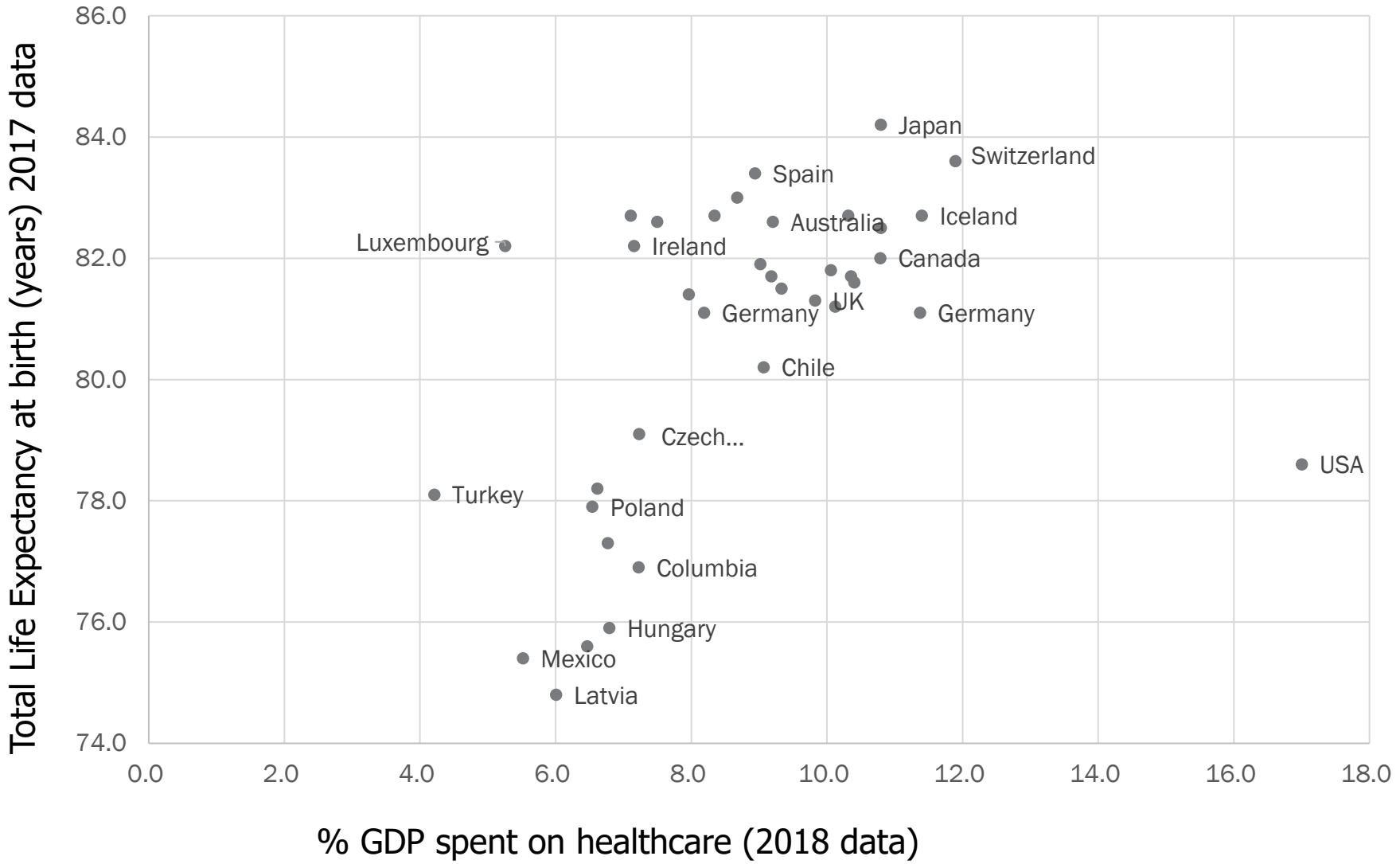
Cost of health care and life expectancy



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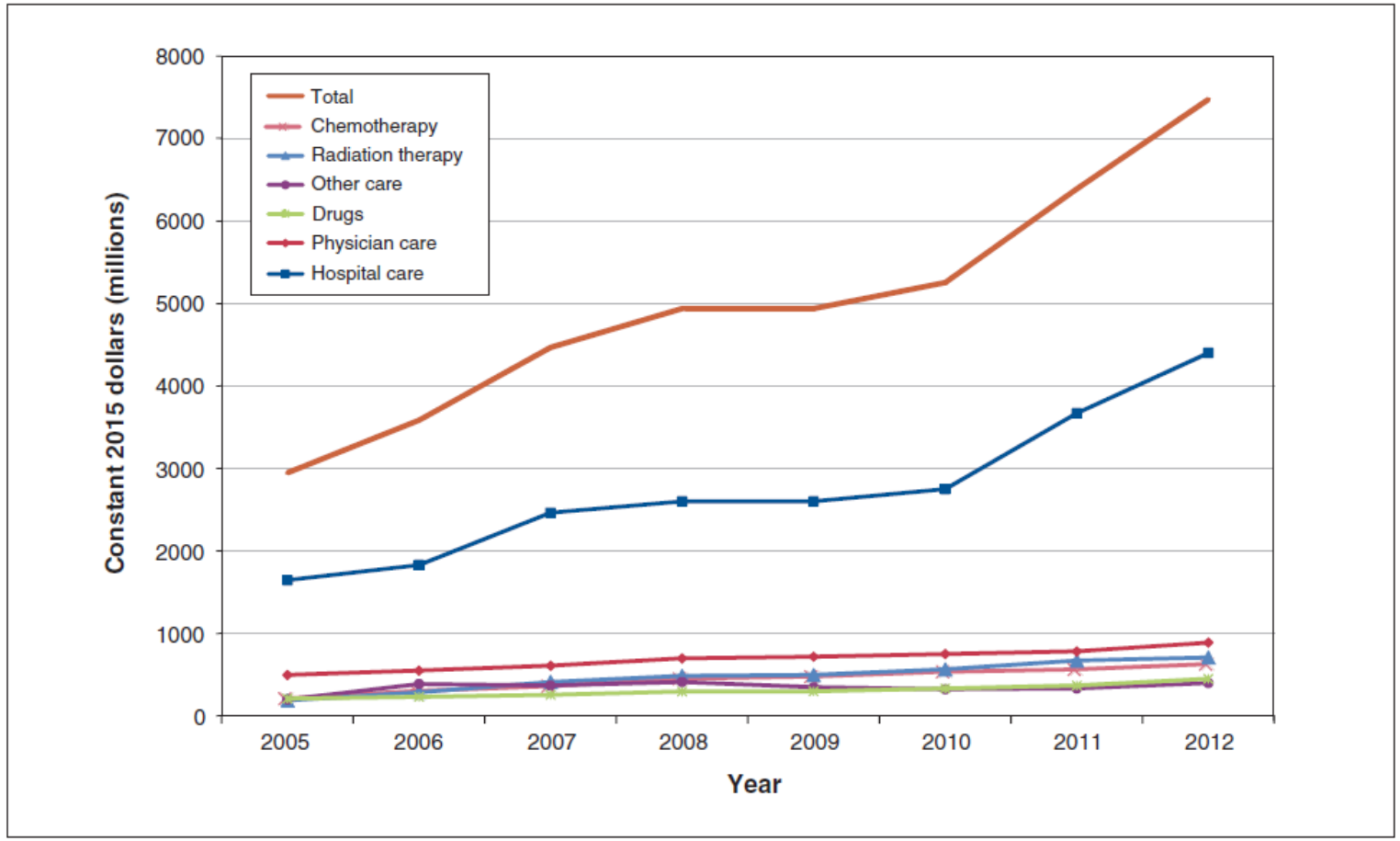
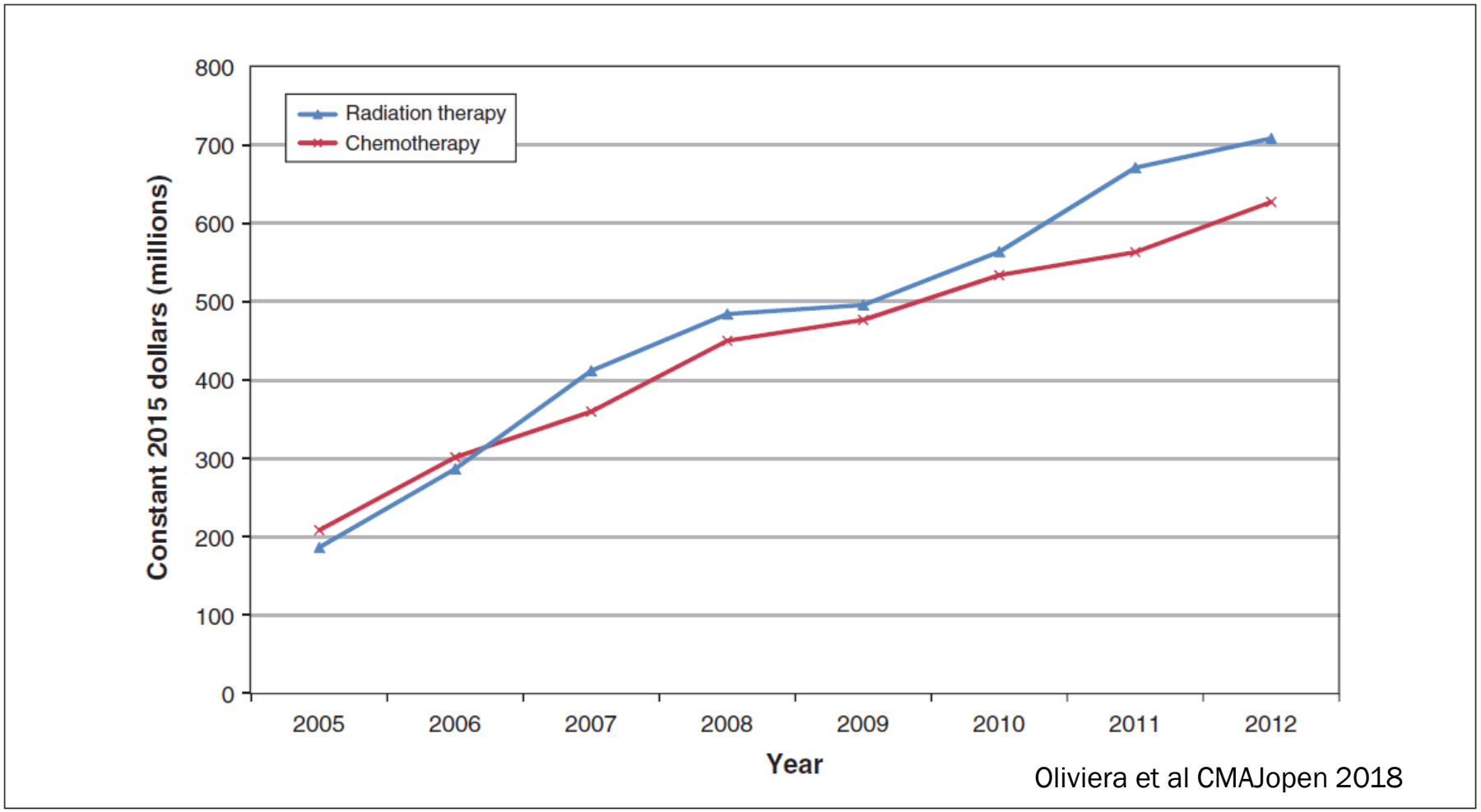
Created 2020Nov9 using OECD 2020 statistics available online

cmajOPEN
Research

The economic burden of cancer care in Canada: a population-based cost study

Claire de Oliveira MA PhD,* Sharada Weir MA DPhil,* Jagadish Rangrej MSc MMath, Murray D. Krahn MD MSc, Nicole Mittmann MSc PhD, Jeffrey S. Hoch MA PhD, Kelvin K.W. Chan MD PhD, Stuart Peacock MSc DPhil





Oliviera et al CMAJopen 2018

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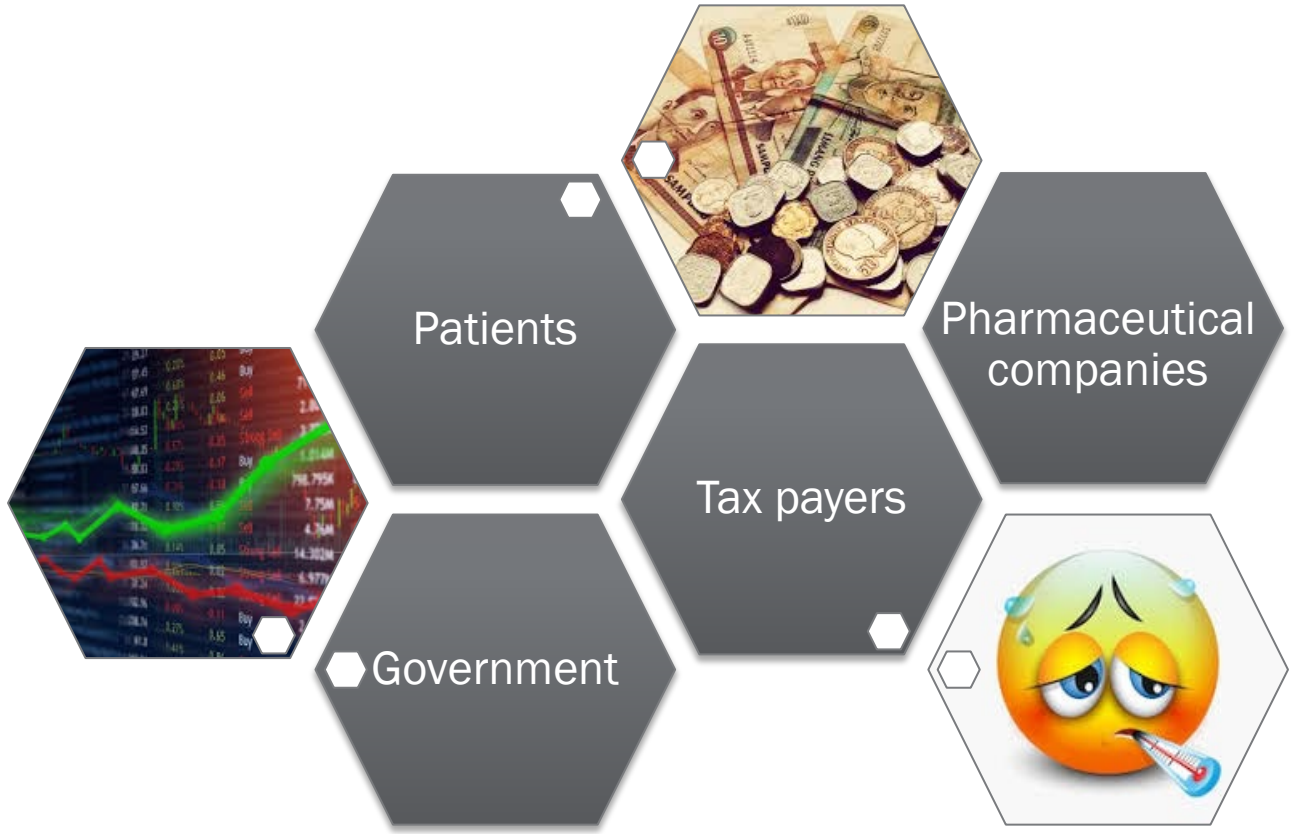
Perspectives on rising health care costs



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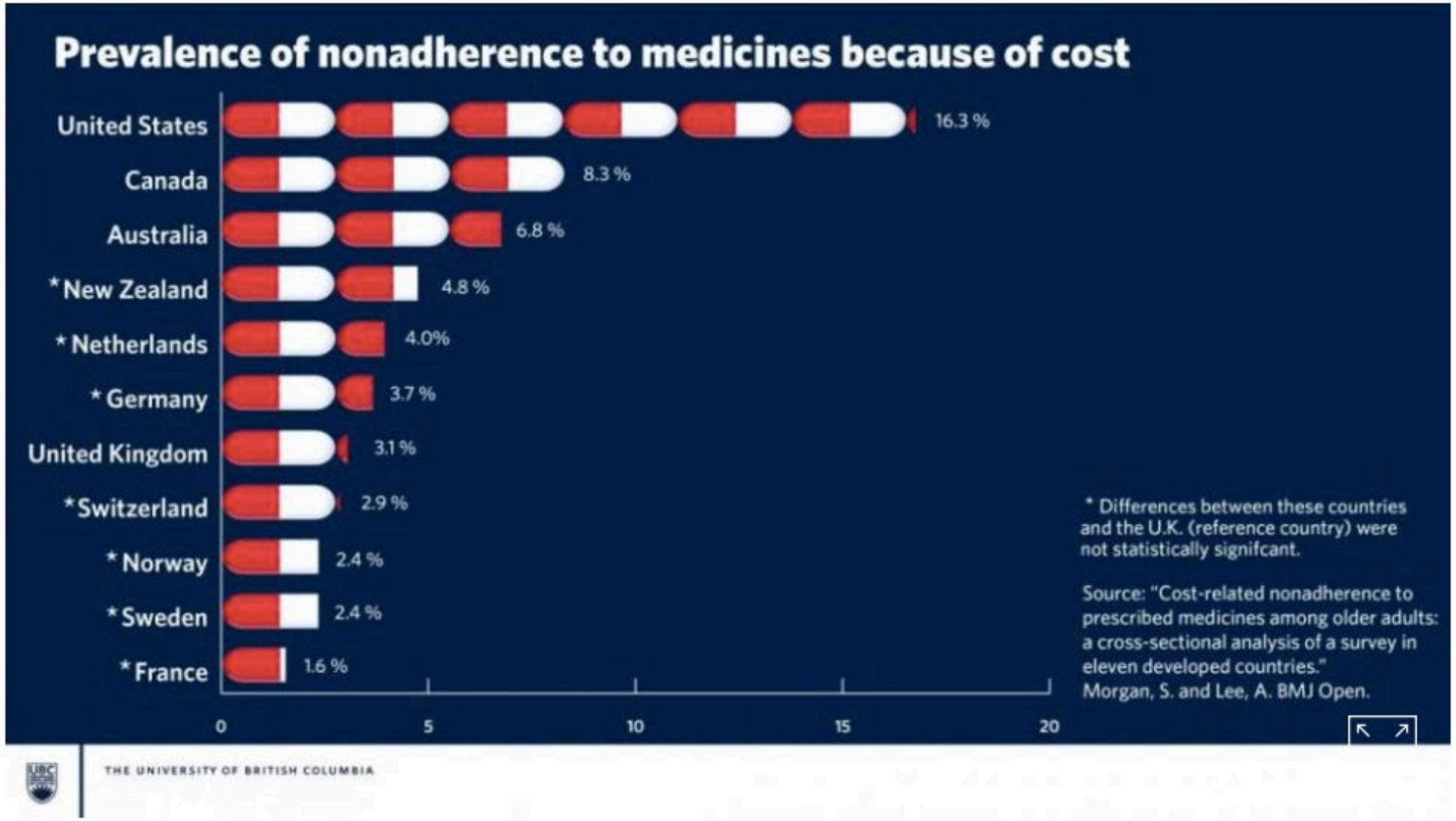

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https://www.upi.com/Health_News/2017/02/01/Seniors-in-US-Canada-skip-prescriptions-due-to-cost/5081485956011/ accessed 2019Nov10 07.33

Perspective on Value

Dr Saltz discussed the difference between value and benefit and that in assessing the value of any therapy, downsides such as toxicity have to be taken into account, as does the cost of the drug.

> These drugs cost too much.
>
> Dr Leonard Saltz

Nivolumab costs $28.78 per mg of drug, whereas ipilimumab costs $157.46 per mg.

"To put that into perspective, that's approximately 4000 times the cost of gold," he commented.

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EDITORIAL

CAR T-cells: costs, comparisons, and commentary

There is understandably tremendous excitement for these therapies that clearly demonstrate meaningful remissions in some individuals with refractory disease. However, huge challenges abound; not least, how healthcare systems can afford these potentially lifesaving treatments. The two CD19-specific CAR T-cell products currently approved by the US Food and Drug Administration, axi-cel and tisagenlecleucel (Kymriah, Novartis) are priced amongst the most expensive cancer therapies to date, $373,000 and $475,000,

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Hay A, Cheung M. Med J Econ 2019

Antibiotic therapy for Helicobacter pylori associated gastric MALT lymphoma

Standard triple therapy:

Pills for each dose on Day 1-10

Rabeprazole (20mg) Amoxicillin (1g) Clarithromycin (500mg)

Eradication of H. pylori bacteria with antibiotics leads to complete remission of lymphoma in 69-90% of cases

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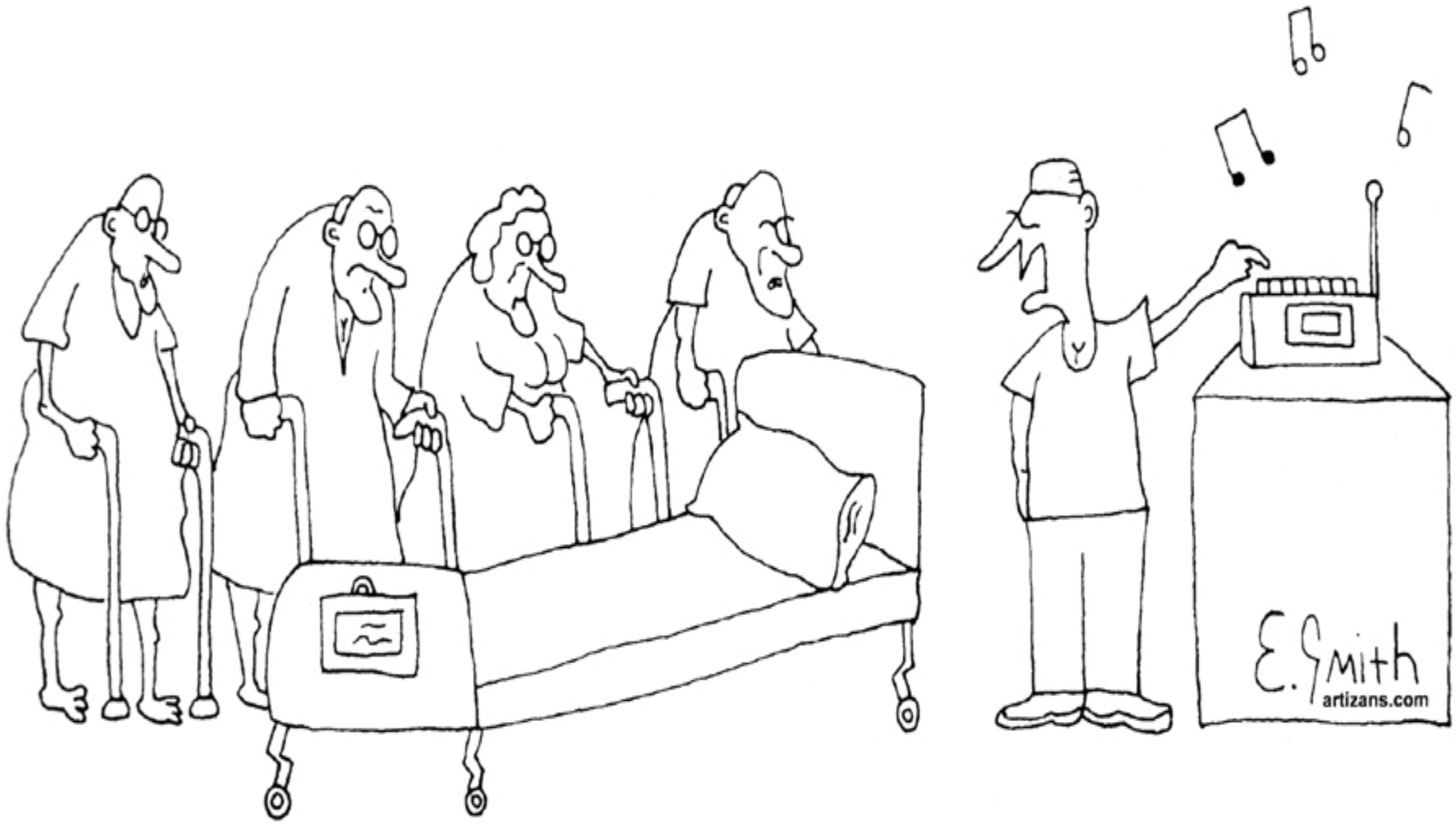
Nakamura, Gastroenterol Clin North Am 2015



"First one on when the music stops gets today's hip operation."

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What
if anything
can clinical trial researchers to do to help?

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Economics and Cancer

- New treatments that improve outcome should be adopted
- But with limited resources, economic constraints factor into resource allocation, in order to maximize population health

- US - 3 pillars of FDA approval of novel interventions:
  1. **Safety**
  2. **Mechanism of action**
  3. **Clinical efficacy**
  4. **Cost-effectiveness**

  expression of an intervention's cost in relation to its benefit

  additionally considered in Canada

Incremental Cost Effectiveness Ratio (ICER)

- Δ cost between option A and option B/ Δ benefit

- Treatment A costs $10,000 - B $8,000
- A improves survival by 1 year, quality-adjusted survival by 0.8 yrs

- ICER – $2,000/LYG; $2,500/QALY

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Higgins & Harris 2012

Table 1
Comparison of different types of economic evaluations

Type of Evaluation	Measurement of Costs	Measurement of Benefits	Summary Measure
Cost-minimization analysis	Dollars	None	Dollars (difference in cost between alternatives)
Cost-effectiveness analysis	Dollars	Natural units/clinical outcome (eg, life-years gained, cases of ventilator-acquired pneumonia avoided)	Cost-effectiveness ratio (eg, dollars per life year gained)
Cost-utility analysis	Dollars	Healthy years or QALYs	Cost-utility ratio (eg, cost per QALY)
Cost-benefit analysis	Dollars	Dollars	Net gain or loss in dollars

Components of an Economic Analysis

- Select type of analysis (CUA, CEA, CMA)
- Perspective – Societal; Payer (government), Patient
- Prospective or Retrospective or Administrative Data Collection
- Costs – direct and indirect medical, lost productivity
- Time Horizon – lifetime; duration of clinical trial
- What about after trial? Adjuvant – late effects, relapse and treatment
- Outcomes – survival in Phase III trial; (what about PFS in phase II?)
- How do you value survival with cancer vs. cancer-free? Utilities, QALY
- What about value of PFS, RR? Time with toxicity?
- What comparator(s) should be used?
- Discounting – used for valuation of future costs, benefits
- Uncertainty – 95% confidence intervals, sensitivity analyses

Quality Adjusted Life Year (QALY)

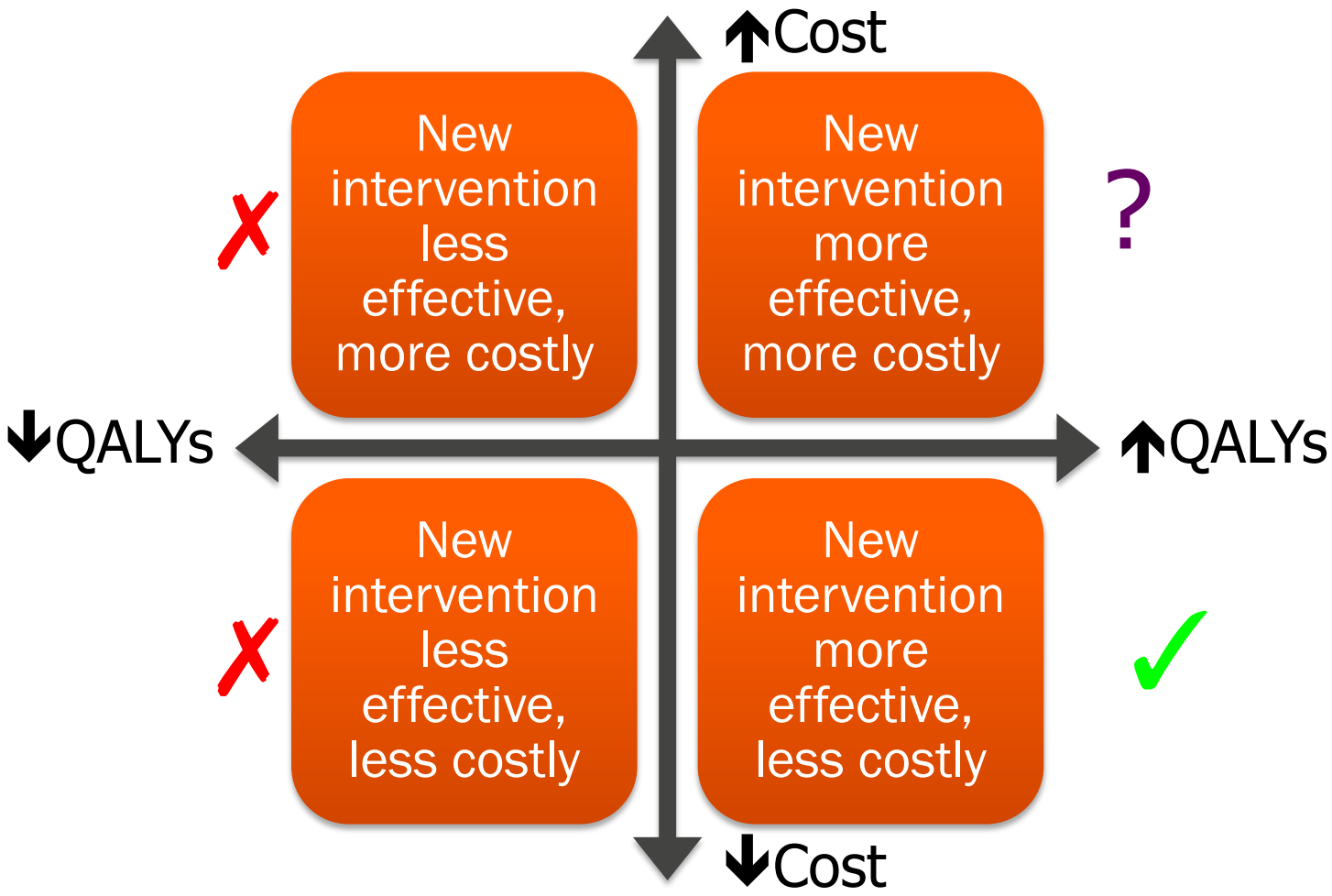
- Integrates mortality and morbidity
- QALY= duration of health state * utility score during that health state
- 1 year with disease = fraction of a healthy year
- Considers impact on quality of life
- Considers impact of toxicity

Health Preference (Utility)

- Measure of health preference
  - 1-perfect health
  - 0-death
  - Average Canadian 0.92-0.96
  - Changes according to disease state

- Standardized tools available to measure
  - Direct-Time Trade Off, Standard Gamble
  - Indirect-HUI, EQ5D, VAS

Adopting a New Technology



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Laupacis *et al*. CMAJ 1992

League Table

INTERVENTION	COST/life-yr gained
Bone marrow transplant	$220,000
Inpatient hemodialysis	$ 54,000
Neonatal ICU	$ 30,900
Automoblie airbags	$ 20,000
Treatment of mild hypertension	$ 19,100
Treatment of severe hypertension	$ 9,400
Bypass surgery (left main)	$ 4,200
Mandatory smoke detectors	$ 1,300
Smoking cessation counselling in men	$ 705

CEA Criteria for Determining if a Clinical Trial is Appropriate for an Economic Evaluation

- New intervention anticipated to have only a modest therapeutic benefit in a potentially large patient population
- Therapy potentially very costly
- High degree of uncertainty about economic impact of treatment
- Economic evaluation may yield important information in determining routine practice (e.g. equivalence trial)
- Economic data will assist future economic evaluations
- For intergroup trials, suitable number of Canadian patients (100)

Evans et al Chronic Dis Prev 2003

CCTG economic analyses examples

Radiation Oncology

Trial Spotlight

An economic analysis of SC24 in Canada quantified the incremental cost-effectiveness of stereotactic body radiation therapy (SBRT) compared to chemoradiotherapy (CRT) in individuals with spinal metastases.

SBRT has upfront costs compared to CRT. However within the Canadian health care system, SBRT with 2 fractions is likely to be cost-effective relative to CRT. In patients randomized to initially receive SBRT, the total cost for the base case of SBRT was $2,869CAD compared with $2,343CAD for CRT. This produced an incremental cost of $526CAD for SBRT over CRT.
Cost-effectiveness was assessed using a Markov model and took into account observed survival, treatments costs, retreatment, and quality of life over the lifetime of the patient.

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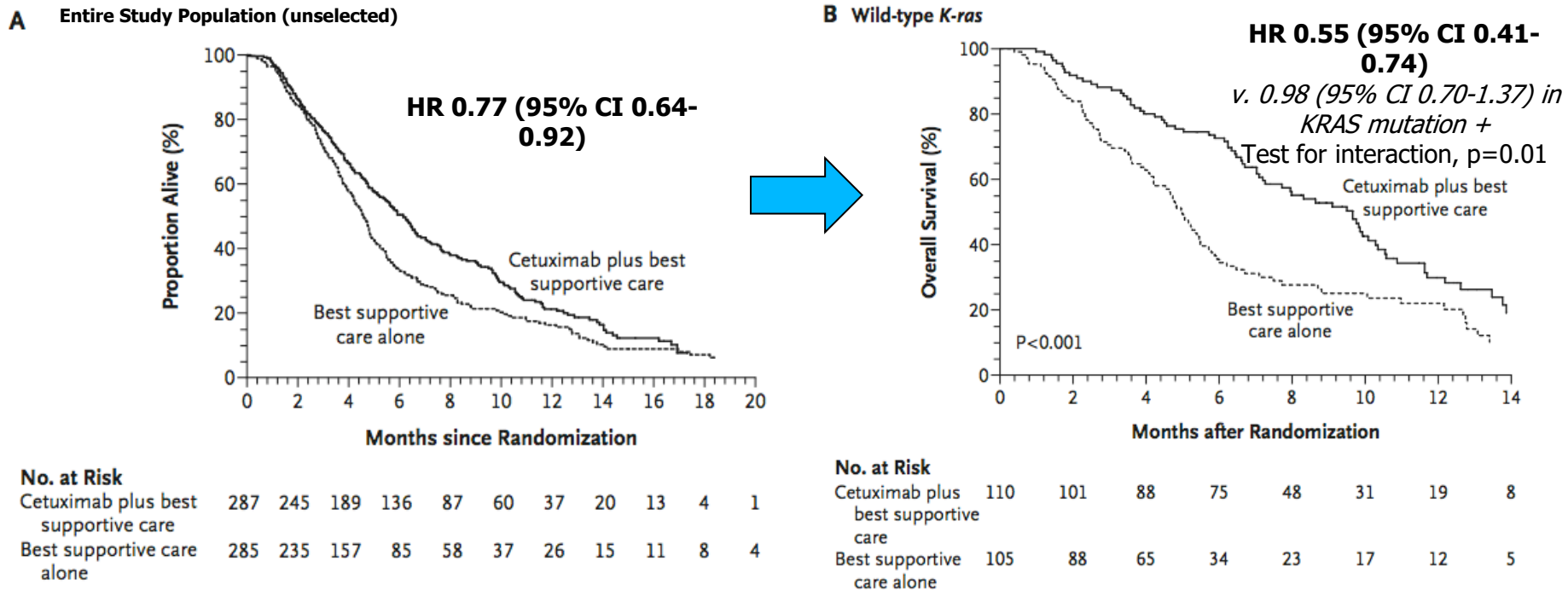
Kerba, Int J Radiat Oncol Biol Phys, 2023

Surgical Oncology

- Cost-effectiveness analysis of simple hysterectomy compared to radical hysterectomy for early cervical cancer from the CCTG CX.5 “SHAPE” phase III clinical trial
- Simple hysterectomy was more effective and less costly than radical hysterectomy.
- Average lifetime costs were $20,044 and $21,714
- Average gains were 3.55 and 3.53 QALYs for simple and radical hysterectomy, respectively.
- Dr. Janice Kwon Presented at ESGO 2023, manuscript in development

Plante, NEJM 2024

NCIC CTG CO.17: Cetuximab improves survival and quality of life in end-stage advanced colorectal cancer; greatest benefit in KRAS wild type (not KRAS mutant)



- 69% tumour samples (394/572), similar characteristics to overall population
- 58% KRAS wild type of those tested (230/394), 40% of entire study population

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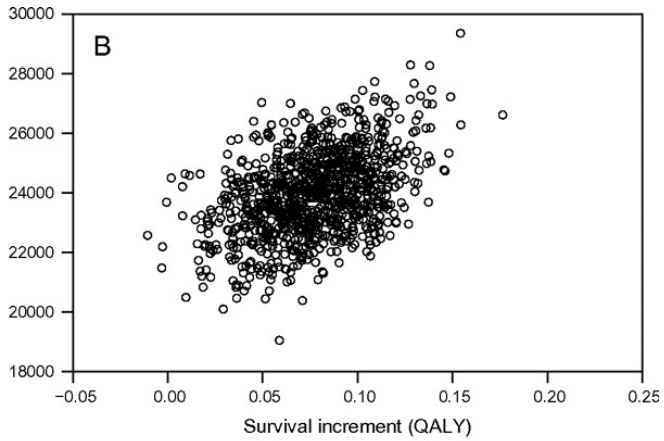
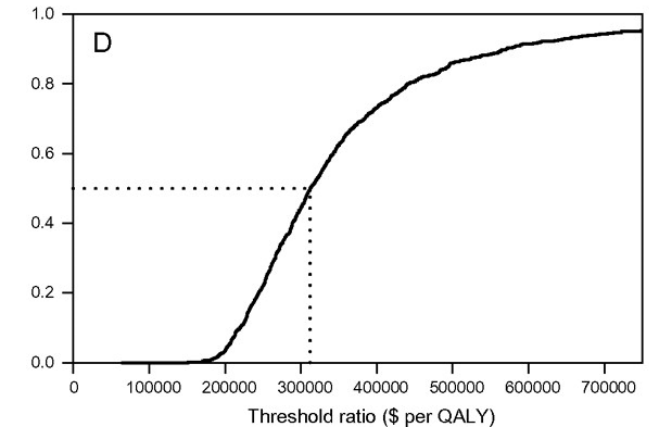
Jonker DJ *et al*. NEJM 2007
Karapetis CS *et al*. NEJM 2008

Prospective Economic Evaluation (resource utilization, HUI3) of Cetuximab Therapy in the entire study population and KRAS wild type subgroup

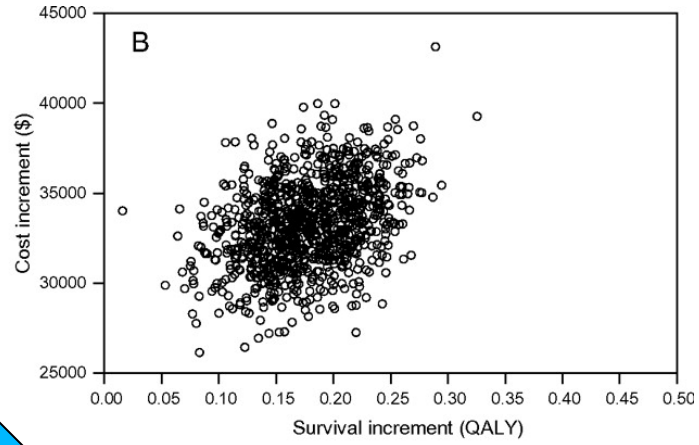
ICUR $300,000/QALY

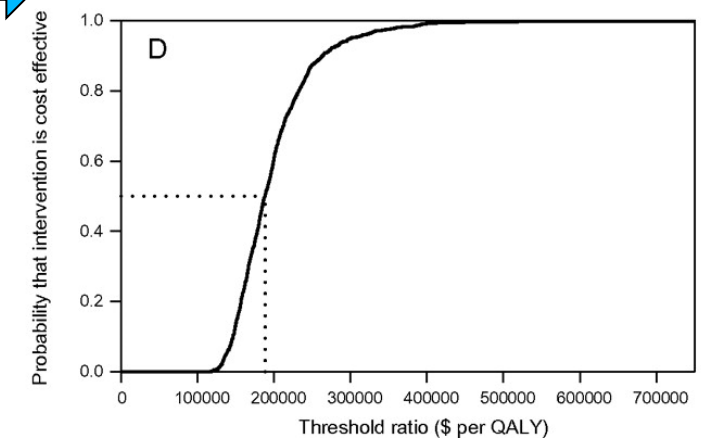




Entire study population (n=572)

ICUR $187,000/QALY





KRAS wild type (n=230)

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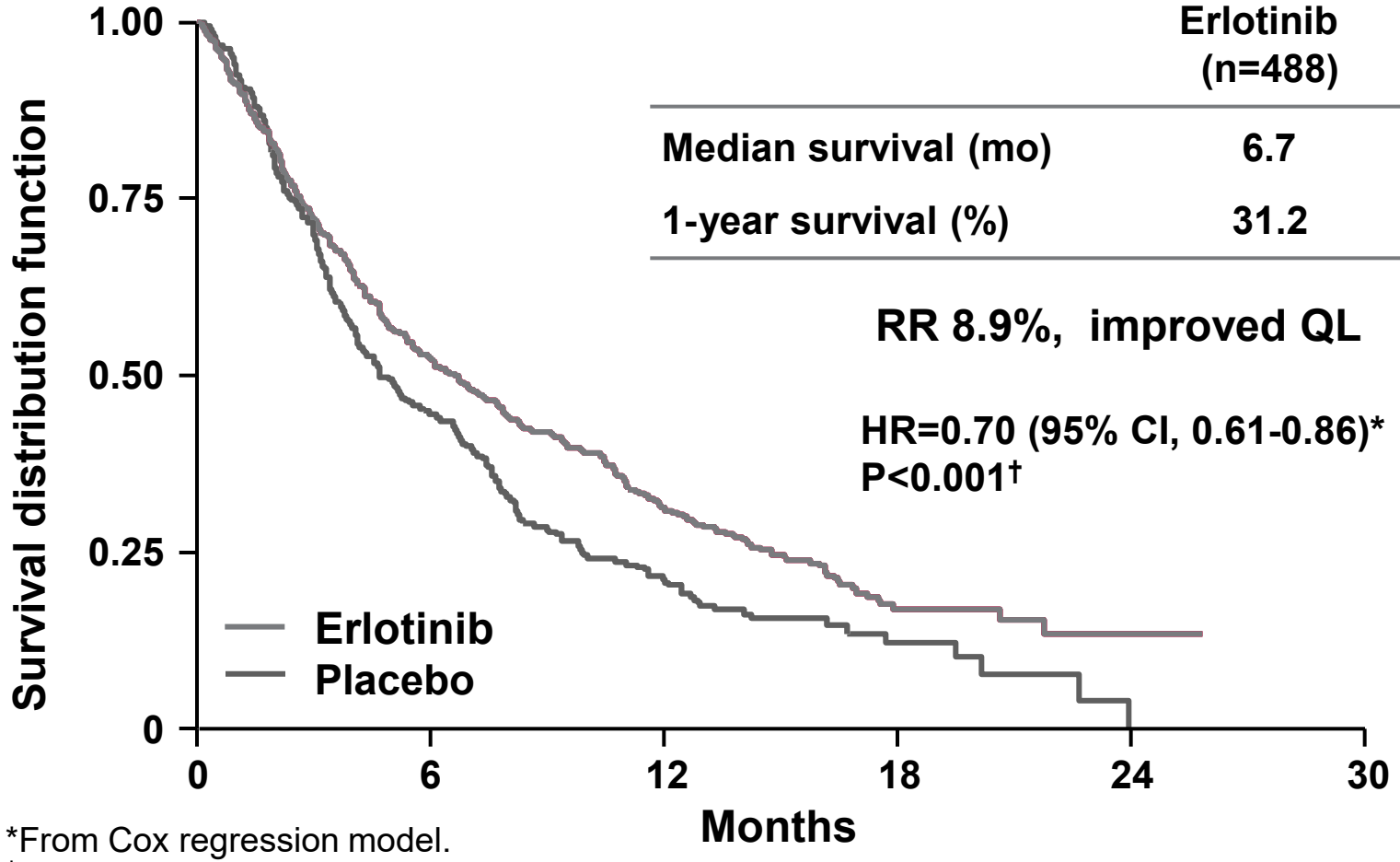
Mittmann *et al*. JNCI 2009

BR.21: Erlotinib vs. Placebo in pretreated advanced non-small cell lung cancer



	Erlotinib (n=488)	Placebo (n=243)
Median survival (mo)	6.7	4.7
1-year survival (%)	31.2	21.5

RR 8.9%, improved QL

HR=0.70 (95% CI, 0.61-0.86)*
P<0.001†

*From Cox regression model.
†From 2-sided log-rank test.
HR = hazard ratio.

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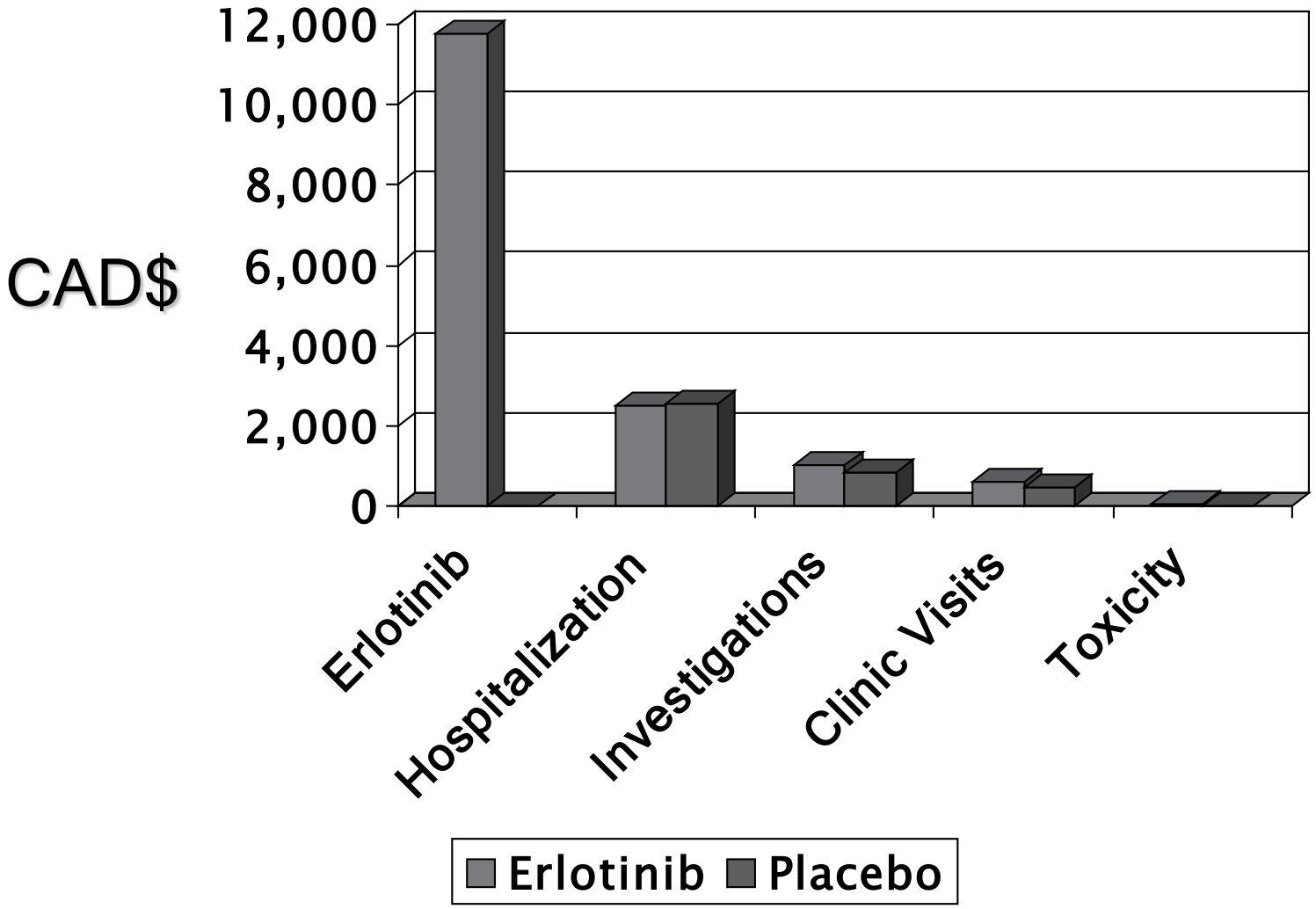
Shepherd *et al*, NEJM

Mean Costs per Treatment Arm



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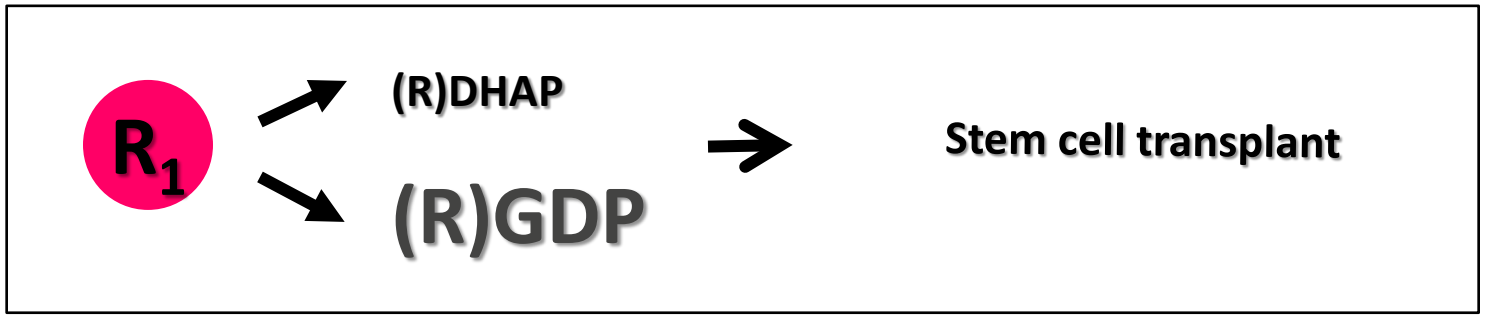
Patients with relapsed or refractory aggressive lymphoma



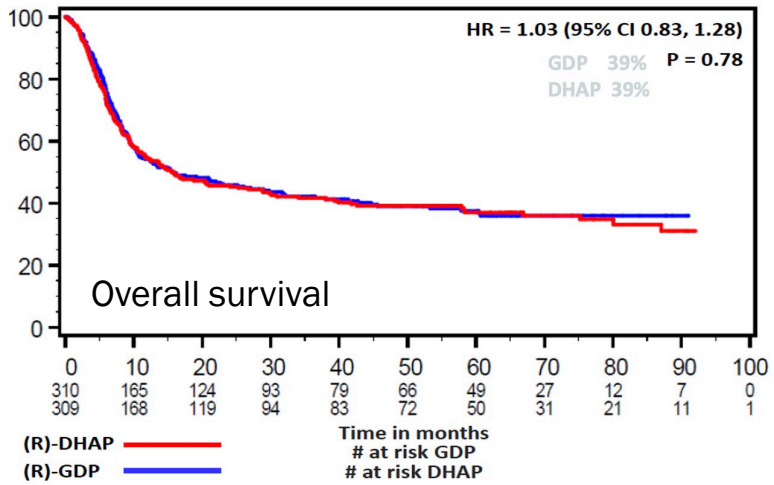
Non-inferiority design

Hypothesis: Equally efficacious, less toxic, less costly
Co-Primary endpoints: response rate and transplantation rate

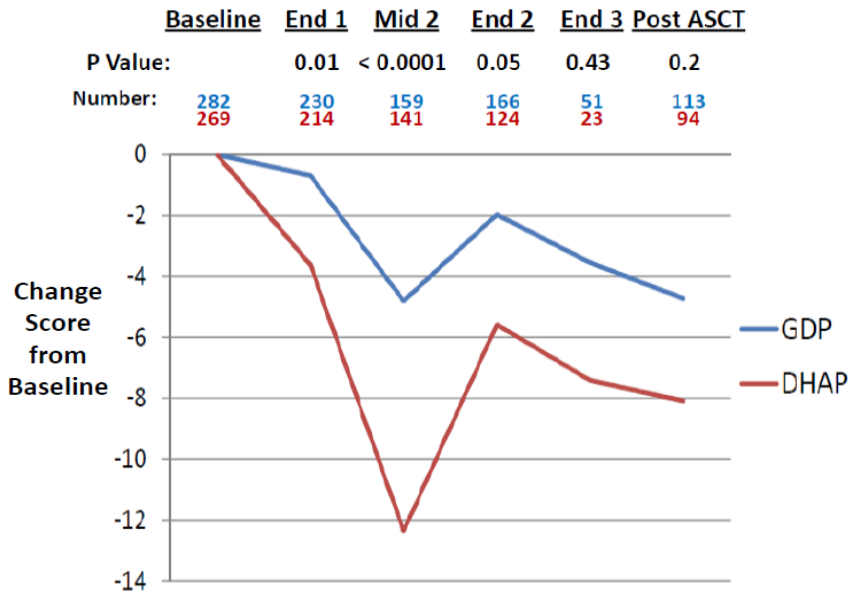
LY.12 Outcomes

Efficacy:
GDP is non-inferior to DHAP

N=619	(R)DHAP (%)	(R)GDP (%)	P-value
Response rate non-inferiority	44	45.2	0.005
Transplantation rate superiority	49.3	51.8	0.49



Quality of life:
GDP is superior to DHAP



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Embedded Economic Analysis Question Options

•Cost-minimization analysis from payer perspective

What is the difference in cost associated with administration of (R)DHAP or (R)GDP chemotherapy to patients with relapsed or refractory aggressive lymphoma who are fit for autologous stem cell transplantation?

•Cost-utility analysis from payer perspective*

In the same population, how does cost per quality-adjusted life-year differ between arms?

•Cost-utility analysis from societal perspective

Include lost productivity and caregiver costs

Design

- Public payer perspective
- ITT analysis
- Canadian subset of patients
- Resource utilization data derived from case report forms
- Direct medical costs applied to resource utilization data
  - Costs obtained from Canadian/provincial databases
  - Time-horizon (randomization to mobilization)
  - 2012 CDN dollars (no discounting)
- Outcomes – survival (discounted at 5%/year)
- Utilities – translated from FACT-G
- Sensitivity analyses

Dobrez et al., Val Health 2007

Costs in 2012 Canadian Dollars

	Cost	Source
Hospitalization*	$1144.11 to $1458.07 / day	Ontario Case Costing Initiative
ER visit**	$166.57	Canadian Institute for Health Information Survey 2005
Home visit	$19.91	Ontario Schedule of Benefits Working in Canada
Office visit	$24.46	
Transfusion Red blood cells Platelets Additional OP cost	 $422.47 $355.52 $50.42	 BloodyEasy Canadian Blood Services Sunnybrook Hospital
Concomitant medication	Individually costed	Alberta Health Interactive Drug Benefit List
Chemotherapy DHAP GDP	 $11,161.24 $12,237.01	Ontario Drug Benefit Program Pharmacist salary Cancer Care Ontario

* Limitation: ICU admissions not known

** Adjusted for inflation

} Overhead costs included

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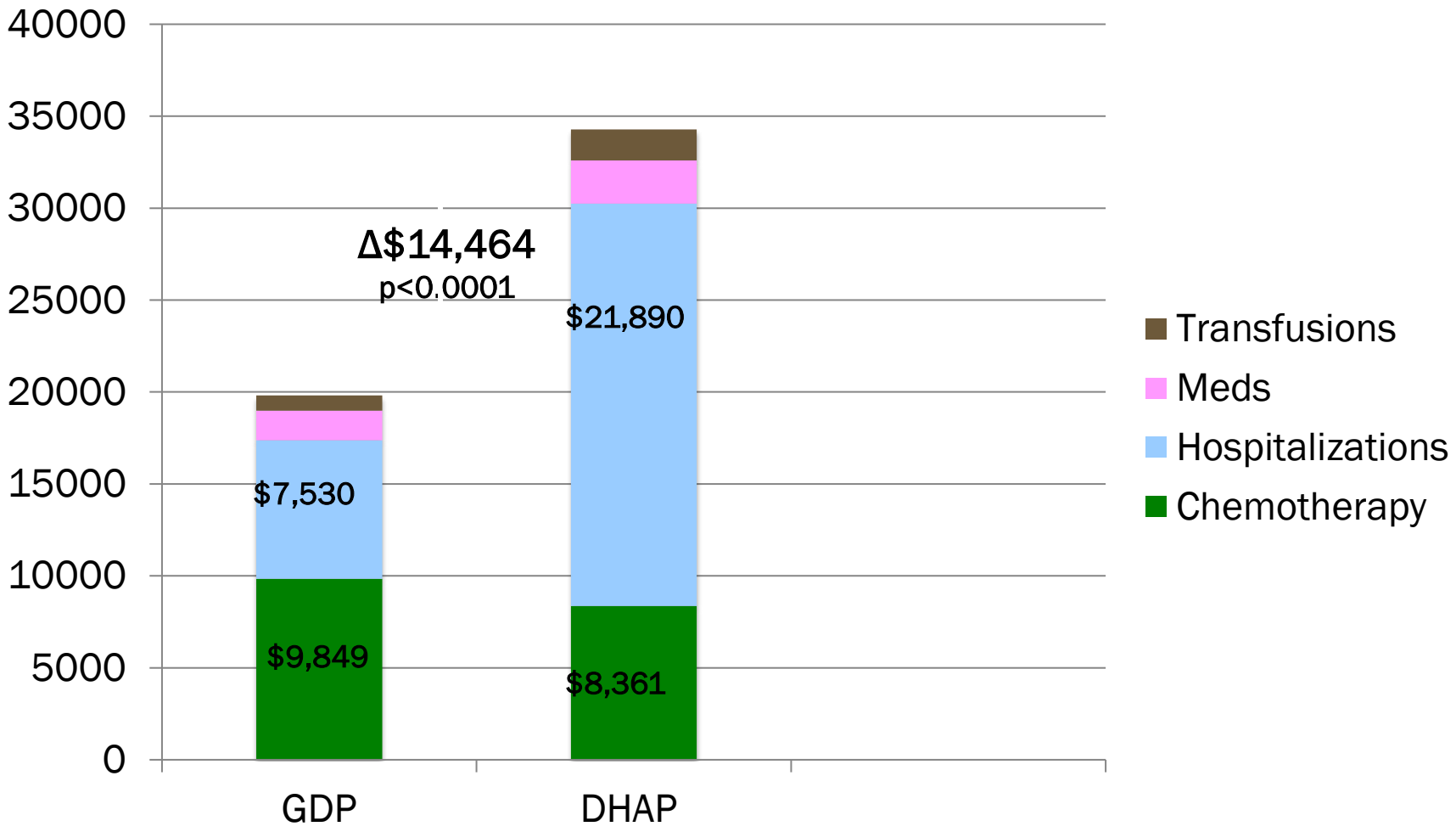
Direct Costs



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Quality of Life: Methods

Use of *Functional Assessment of Cancer Therapy – 0-4 point scale*

- FACT-G 27 items
- FACT-CNS 12 items
- FACT-LYM 27 items

Assessed at:
Baseline
End of cycle 1
Middle of cycle 2
End of cycle 2 (and 3 if applicable)
1 month post-transplantation

Volume 10 • Number 4 • 2007
VALUE IN HEALTH

Estimation of Patient Preference-Based Utility Weights from the Functional Assessment of Cancer Therapy—General

Deborah Dobrez, PhD,[1] David Cella, PhD,[2] A. Simon Pickard, PhD,[3] Jin-Shei Lai, PhD,[2] Angel Nickolov, MS[4]

[1]School of Public Health, University of Illinois at Chicago, Chicago, IL, USA; [2]Center on Outcomes, Research, and Education, Evanston Northwestern Healthcare, Evanston, IL, USA; [3]Center for Pharmacoeconomic Research and Department of Pharmacy Practice, College of Pharmacy, University of Illinois at Chicago, Chicago, IL, USA; [4]Mallinckrodt/Tyco Healthcare, St. Louis, MO, USA

- Require scores for questions #1 (PWB energy), #6 (PWB ill), #21 (FWB work), #23 (FWB enjoy life)
- Utility = 1 +
- (-0.2222 if q1 = [3,4] or -0.1137 if q1 = [1,2]) +
- (-0.1537 if q2 = 4) +
- (-0.0431 if q3 = [0,1]) +
- (-0.1254 if q4 = [0,1] or -0.0641 if q4 = 2 or -0.0345 if q4 = 3)

Primary Outcome – Cost-utility

	GDP	DHAP	Difference
Cost	**$19,961**	$34,425	**- $14,464** (-20,250 to -9,726; p<0.0001)
QALYs	**0.161**	0.152	**+0.01 QALYs** (p=0.146)
ICER			**GDP is dominant**

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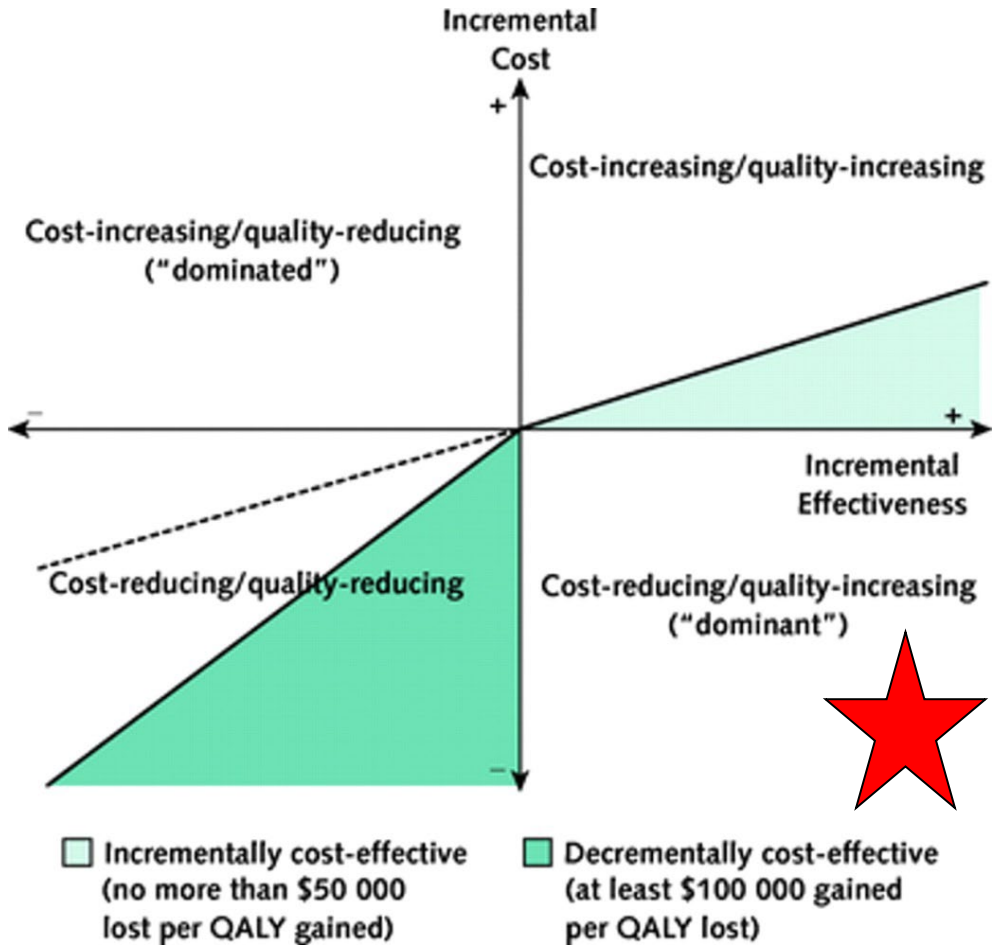
LY.12 results on cost-effectiveness plane



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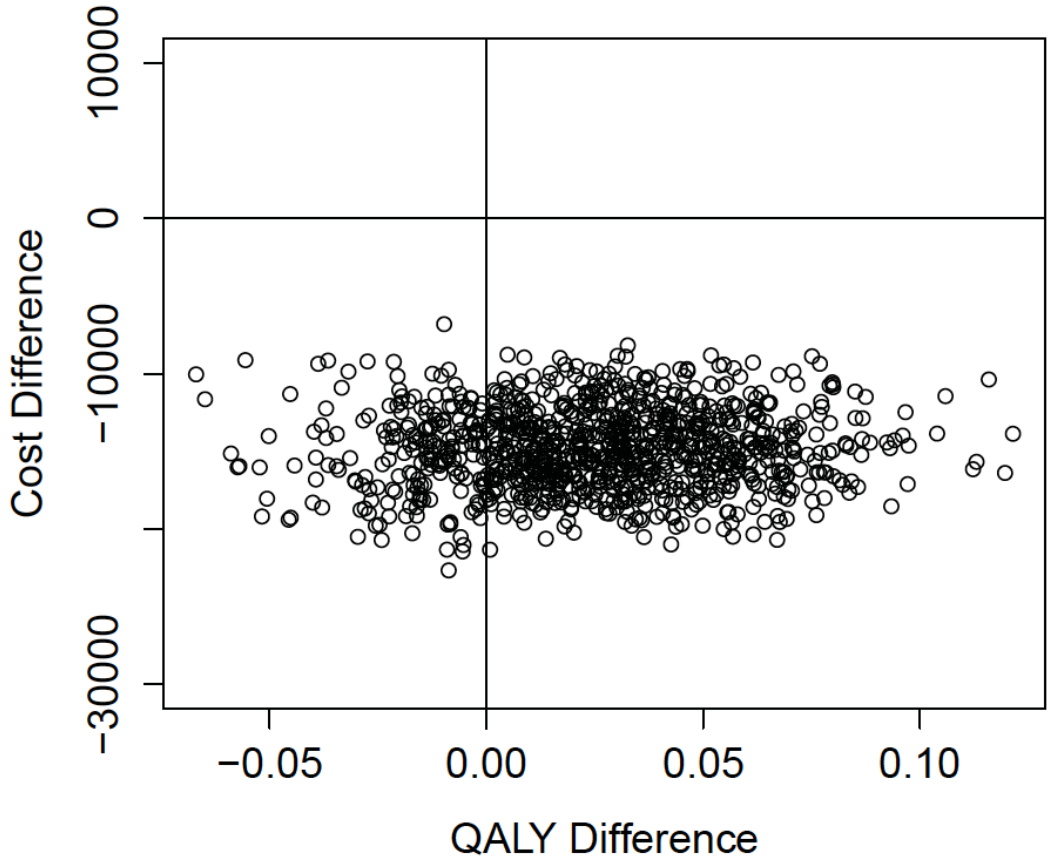
Sensitivity Analyses



Varying
Time horizon
Costs
Survival
Discounting
Bootstrapping

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Wrapping up

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If adding health economic analysis to your protocol

Consider with support

- Perspective: payer, patient, society
- Analysis:
  i. Cost minimization - $ difference
  ii. Cost effectiveness - $ per life year gained
  iii. Cost utility - $ per quality adjusted life year gained
  iv. Incremental cost effectiveness ratio = $\frac{\text{difference in cost}}{\text{difference in benefit}}$
- Time horizon
- Cost components

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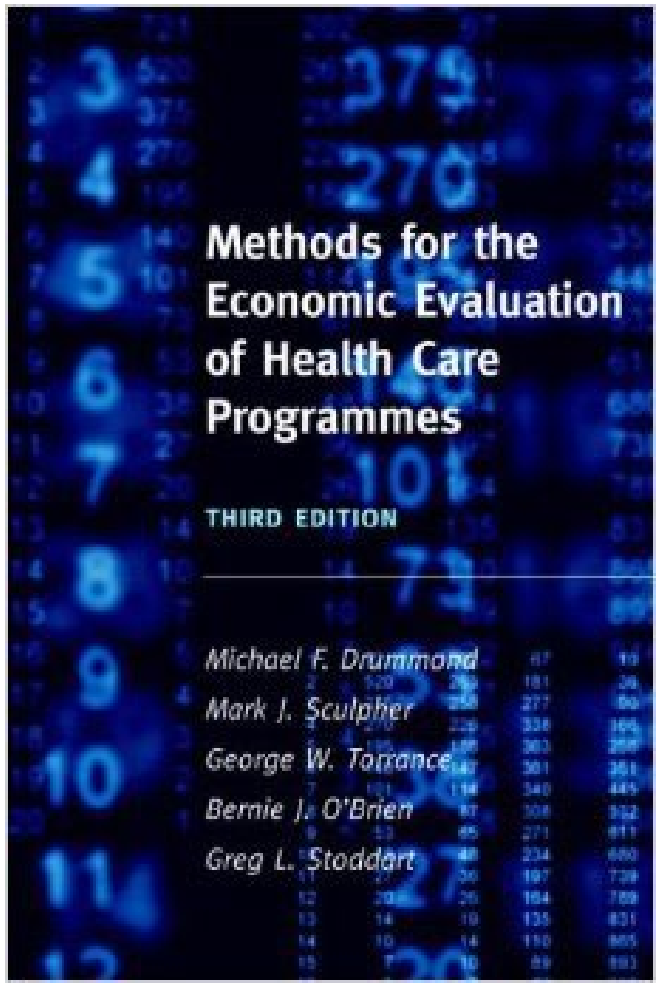
Economic Analyses in Clinical Trials

- Important addition to strengthen, complement results of ongoing clinical trials
- Helps clinicians, patients and policy-makers interpret value of novel interventions
- Critical part of Canadian oncology drug funding process (pan Canadian Oncology Drug Review)
- Timely economic evaluation of interventions may facilitate uptake of novel therapies

Optional further reading



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